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1. Livingston, S., and Petersen, D.: New England J. Med. *254*:327 (Feb. 16) 1956.
2. Pence, L. M.: Texas State J. Med. *50*:290 (May) 1954.
3. Berman, B. A.: Am. J. Psychiat. *112*:541 (Jan.) 1956.

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TO OUR SUBSCRIBERS AND CONTRIBUTORS

SUBSCRIBERS and contributors to this journal have undoubtedly noticed some deviation from our usual publishing quality in the July and August and September issues. In particular, authors have had to correct very bad proofs in less than adequate time for careful reading. Subscribers must have detected an unusual number of typographical errors which were not corrected from the galleys. A most disturbing fact was the late mailing of these issues. Many of our authors and readers were quick to realize that such a departure from our usual standards could be due only to abnormal conditions, and we feel that these conditions need to be explained.

On April 23, 1956, the American Medical Association concluded negotiations for a contract with the Baird-Ward Printing Company, Inc., Nashville, Tenn., to print the American Medical Association Specialty Journals. Under the terms of the contract, the Baird-Ward Printing Company, Inc., was to begin with the July issues.

A transfer of a printing operation requires that many details be considered and many adjustments be made. A contract as large as this involved expanding a work force with skilled operators, not always readily available; installing additional machinery and type equipment not obtainable on short notice, and scheduling nine journals so as to coordinate their production with other jobs in the plant. Editorially, it meant increased pressure upon editors to meet an advanced schedule, the development of a common interpretation of editing procedures between typesetter and manuscript editor, and the working out of communications between the Editorial Office, printing plant, authors, and readers.

All this was a Herculean task in view of the short period of time allowed for the transfer. Obviously, substandard results could not be avoided. While a contributor or a reader is justly concerned with his individual article or copy, it is hoped that the realization of the many ramifications of the transfer will soften criticism of the initial effort, performed under an entirely new set of production conditions.

Many of the early problems have been eliminated. Others are being solved daily. The efforts of the editorial and manufacturing staffs are directed toward an improvement over what our readers have been offered in the past. Publication dates will be improved, and plans are progressing to make our subject contribution more essential to the profession.

We trust that a better understanding of the circumstances will enlist your patient indulgence in our efforts to return to normal publishing conditions and to keep a promise of a better product.

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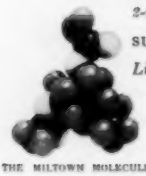

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Section on NEUROLOGY

Cerebrospinal Fluid Thrombocyte-Agglutinating Substance in Multiple Sclerosis

IB PERSSON, Copenhagen

Introduction

The purpose of this work is to find out whether in multiple sclerosis it can be demonstrated that there are changes in the cerebrospinal fluid which may explain why plaques seem to occur at definite sites of predilection, that is, around the small veins in the central nervous system and periventricularly.

Cruveilhier [1] was the first to compare the areas of sclerosis with the results of embolism. Later, Rindfleisch [2] stressed the connection between plaques and blood vessels; however, he was not of the opinion that the plaques were formed as a result of circulatory disturbances alone. Charcot [3] described vascular obstruction. Ribbert [4] considered he had demonstrated that blockage of the arteries in the central nervous system by white cells occurs, although his investigations do not confirm this claim. Williamson [5] emphasized the significance of venous thrombi but gave no further details. Borst [6] formulated a special vascular theory in that he stated the belief that lymphostasis played a prominent role in plaque formation. In their investigations, Schuster and Bielschowsky [7] found changes in the blood vessels and accumulation of white cells as well; similarly, Strähuber [8] described leucocyte emboli occurring partly in plaques and partly in pial veins, where the leucocytes and red blood corpuscles lay embedded in threads of fibrin. Siemerling and Raecke [9] demonstrated by their careful investigations frequent capillary hemorrhages in fresh plaques. Dawson,[10] in his thorough studies, found signs of intravital thrombosis in only a few cases and never the occurrence of organized thrombi, but the conclusion reached from his investigations was that plaques lay in relation to the blood vessels.

While earlier interest has especially centered around the dependence of plaques on the arteries, Putnam and his co-workers * emphasize the significance of the circulatory conditions in the small veins of the central nervous system. In their investigations, they also frequently demonstrated thrombi in that the common type consisted of masses of agglutinated platelets filling the lumen of the vessel, and occasionally the beginning of organization could be detected. Since then others have carried out investigations in order to confirm this theory. However, there is disagreement as to whether thrombi occur

Received for publication Dec. 12, 1955.

From Nørre Hospital (Chief: Prof. E. Jarløv, M.D.), and the Neurological Department of the Municipal Hospital (Chief: Dr. K. Krabbe, M.D.).

* References 11-15.

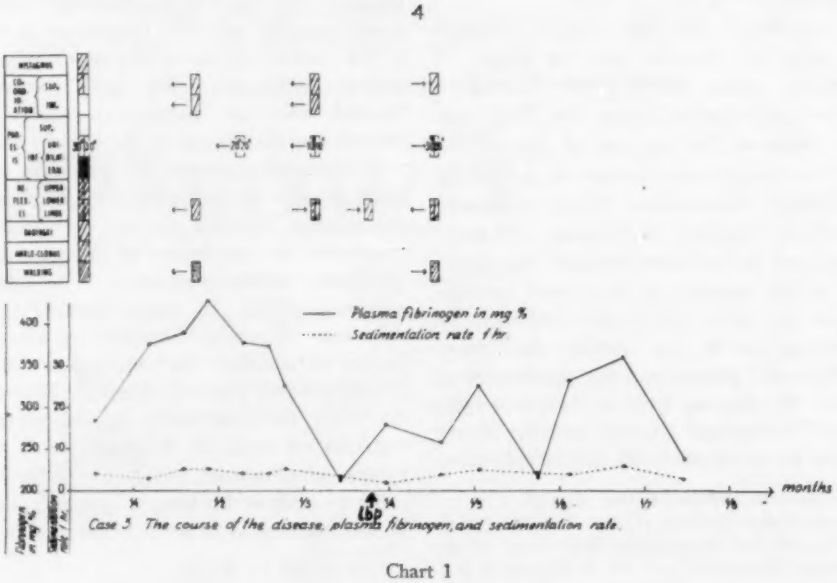
at all. Thus, Zimmerman and Netsky [16] noted absence of thrombi in 50 cases of multiple sclerosis. Macchi's [17] investigations also showed no sign of thrombosis in fresh plaques. Dow and his associates [18] were able to demonstrate thrombi only in exceptional cases; on the other hand, it was their opinion that the supposition that demyelination was entirely without relation to the vascular system was not reliable. By means of thorough studies, Fog [19] showed that plaques lie in relation to the veins, but found thrombi in only a few cases. Broman [20] demonstrated a permanent change in the permeability of the cerebral vessels in the plaques, but he, also, did not find thrombi.

Periventricular sclerosis was described by Charcot,[21] Borst,[6] Strähuber,[8] and Westphal,[22] among others; and the localization has been emphasized by Lhermitte and Guccione,[23] Merle and Pastine,[24] and Schob [25] as being dominant. In his thorough investigations, Dawson [10] found, however, that among his nine cases the periventricular affection was very marked in six, whereas it was only slight in two others and scarcely noticeable in one. At a later date Steiner [26] has once more described the dominant periventricular sclerosis, and Hallervorden [27] claims that it is so characteristic that in its absence one must doubt whether the diagnosis is correct. In the investigation of a larger number of cases, Zimmerman and Netsky [16] found, similarly, that there was a strong predilection for the periventricular regions. This localization claims special interest in relation to the pathogenesis of multiple sclerosis and raises the question whether this localization possibly is dependent upon the presence of the causal agent in the cerebrospinal fluid itself.

The problem is, now, to ascertain whether it is possible to demonstrate in the blood and spinal fluid, in connection with the exacerbations in multiple sclerosis, simultaneous changes which could be considered as explaining why the plaques seem especially to be localized periventricularly and around the small veins in the central nervous system.

Clinical Material

The investigations comprised 10 patients



Case 5. The course of the disease, plasma fibrinogen, and sedimentation rate.

Chart 1

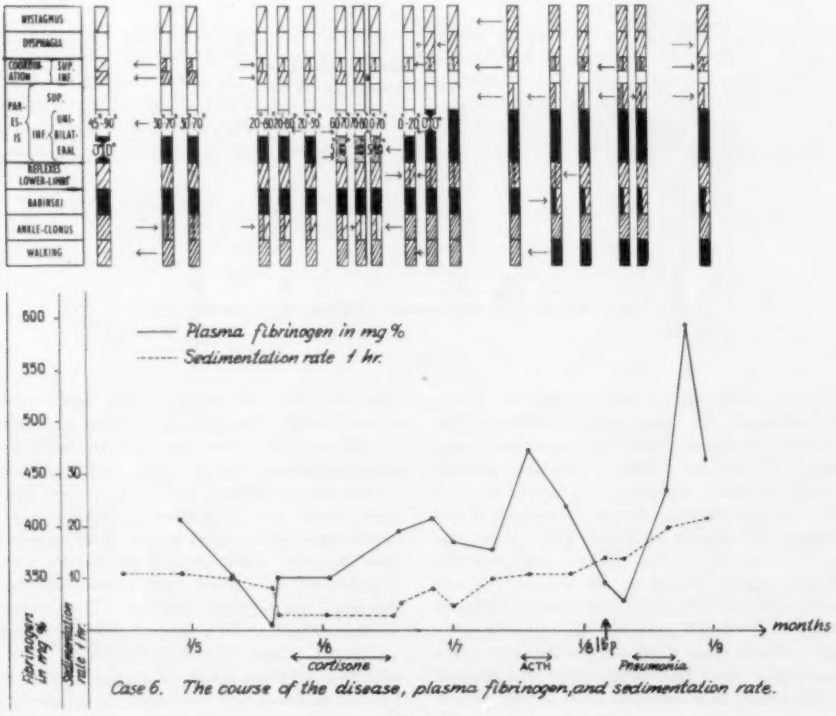
with multiple sclerosis, whose case histories will be stated briefly below.

The neurological condition at different times is shown on the charts, which have been so designed that within each date column the patient must be visualized as facing the examiner, the left half of the date column representing the patient's right side and the right half his left side. The numbers indicate how high the limbs could be lifted. Decreasing hatchure or arrows pointing from left to right indicate improvement of the condition, and the reverse, deterioration. At the points marked with an arrow lumbar puncture was performed. Furthermore, the values for plasma fibrinogen and sedimentation rate are stated.

Summary of Cases

CASE 3 (Chart 1).—A woman aged 38. The patient fell ill at 28 years of age. The first symptom was difficulty in walking. The condition deteriorated through the years, the course being interrupted only by partial remissions. The patient was partially demented. There was gross nystagmus. Ophthalmoscopy showed nothing abnormal. Power was good in both arms. Tonus was slightly increased, and the deep reflexes were brisk, especially on the right side. The finger-to-nose test showed ataxia on the right side. The abdominal skin reflexes were absent. Power was diffusely reduced in the lower limbs. There was spasticity. The reflexes were brisk, especially on the right side, and could be elicited over a wider zone. Moreover, ankle clonus and the Babinski sign were present bilaterally. The patient could not lift her legs together with her knees straight. The gait was very spastic, and she could walk only when she was supported by two helpers.

CASE 6 (Chart 2).—A woman aged 22. She fell ill at the age of 19, the initial signs being left-sided retrobulbar neuritis and paresthesiae in the right hand. The course of the disease had been intermittent, but there had not at any time been a complete remission. On examination slight nystagmus at the extreme positions of the eyes was found. Ophthalmoscopy showed bilateral optic atrophy. The upper limbs were normal, apart from slight intention tremor and slight asynergia on the left side. The abdominal skin reflexes were absent. The



Case 6. The course of the disease, plasma fibrinogen, and sedimentation rate.

Chart 2

lower limbs showed a spastic increase of tonus; brisk reflexes, demonstrable over a wider zone; bilateral brisk ankle clonus and a tendency toward patellar clonus, and a bilateral Babinski sign. There was slight paresis of the right lower limb, which could be raised 45 degrees with extended knee; the left leg could be raised 90 degrees. The legs could not be raised together. The heel-to-knee test showed some ataxia. The gait was slow and very spastic. As shown on the curve, the patient was treated with cortisone (25 mg. four times daily) for a period, and for a later period with corticotropin (10 mg. four times daily); but it was not possible to demonstrate any improvement objectively, and, in addition, the patient felt worse. At the start of the illness, however, the patient had reacted favorably to this treatment. In August, 1952, the patient developed pneumonia, which was treated with procaine penicillin G.

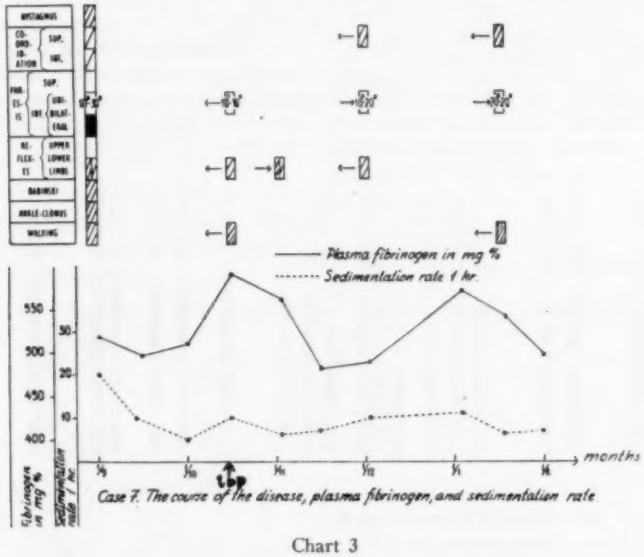


Chart 3

Case 7 (Chart 3).—A woman aged 46. Three years previously she developed a feeling of uncertainty in the lower limbs and experienced some dizziness. During the following year the condition remained relatively stationary, but in the last few months before admission to the hospital there was increasing difficulty in walking. The patient was somewhat euphoric. The speech was staccato. When the patient looked to the left, paresis was demonstrated and nystagmus was present. Ophthalmoscopy showed the presence of temporal optic atrophy. There were slight final uncertainty in the finger-to-nose test and slight dysdiadokokinesia. The abdominal skin reflexes were absent. There was a spastic increase of tone in the lower limbs, and power was diffusely reduced, especially on the right side. The knee jerks were brisk, especially on the right. There were a bilateral ankle clonus and Babinski sign. The heel-to-knee test was performed with terminal uncertainty. The patient could walk with the help of one person.

Case 8 (Chart 4).—A man aged 39. The patient became ill at the age of 24. The disease presented with difficulty in walking; he had special difficulty in controlling his left leg. The course of disease had been one of steady progression, with no marked remissions. At the time when the examinations began, the patient showed some mental depression. There was marked horizontal nystagmus. Ophthalmoscopy showed left-sided temporal optic atrophy. The deep reflexes in the upper limbs were moderately brisk and equal on the two sides. There were slight past pointing in the finger-to-nose test and gross terminal tremor. The power was normal. The abdominal skin reflexes were equal and moderately brisk. The right leg showed slight spastic increase of tone. The deep reflexes were hyperactive, especially on the right, and were demonstrable over a widened zone. There were bilateral ankle clonus and a bilateral Babinski sign. The heel-to-knee test showed ataxia. Each lower limb could be raised alone through 40 degrees with extended knee, with fairly good power, whereas the legs could not be raised together. The patient was unable to stand or walk unless aided by one person.

Case 12 (Chart 5).—A man aged 34. The first symptoms occurred when the patient was 31, in the form of dizziness and headache; the following year the patient complained of loss of power in the

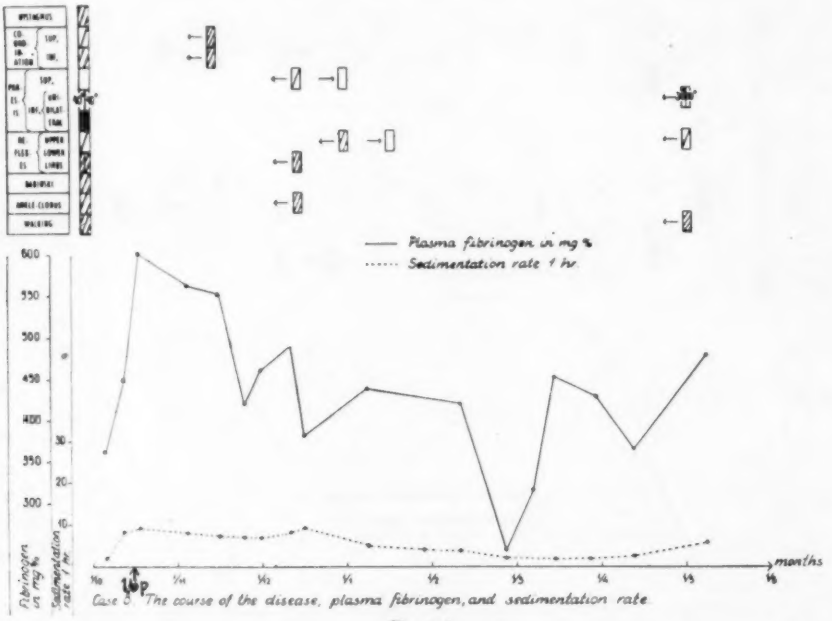


Chart 4

lower limbs. Subsequently the condition progressed rapidly without any considerable remissions. The patient was euphoric. There was gross nystagmus. Ophthalmoscopy showed bilateral temporal optic atrophy. The speech was slightly staccato. There were ataxia in the finger-to-nose test, especially on the right, and dysdiadokokinesia. The abdominal skin reflexes were absent. There was spastic increase of tone in the lower limbs and decreased power. The knee jerks were brisk, with slight preponderance on the left side. There was bilateral ankle clonus, and Babinski's sign was present on

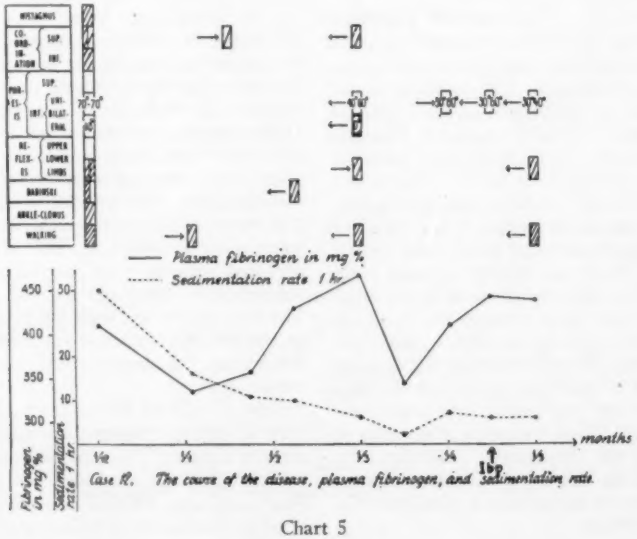
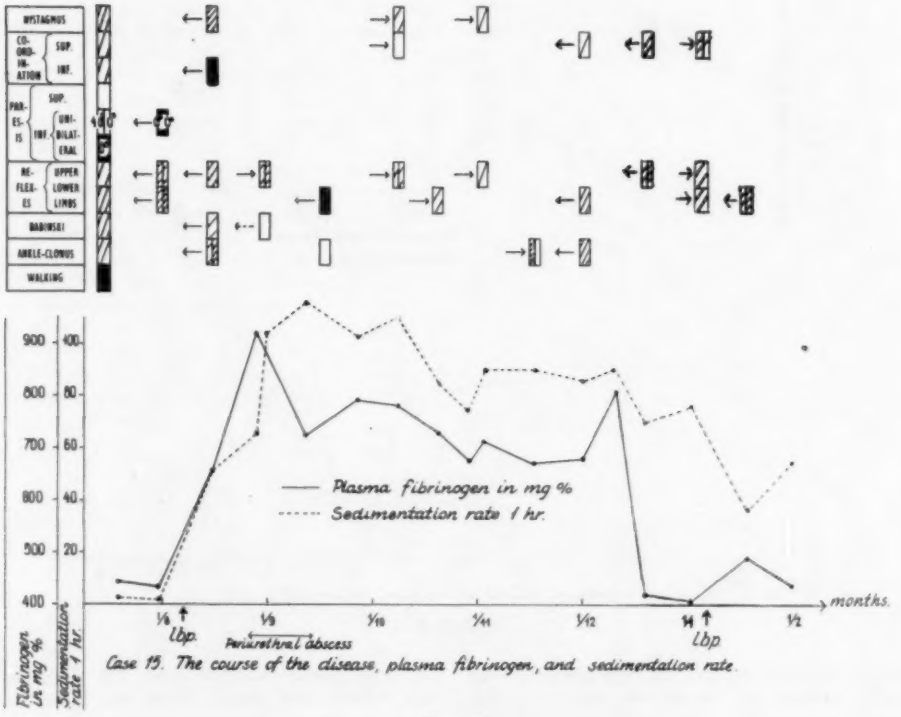


Chart 5



Case 15. The course of the disease, plasma fibrinogen, and sedimentation rate.

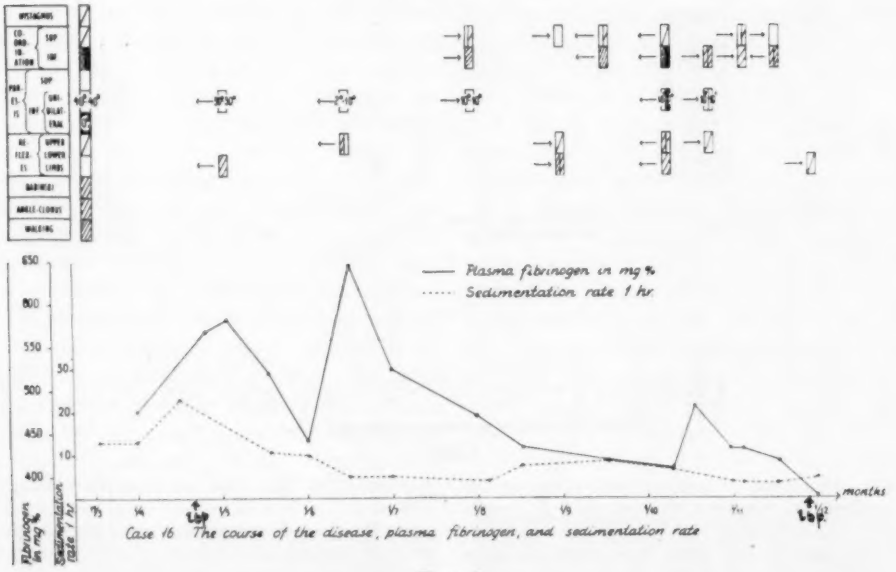
Chart 6

the right side. There was rather marked ataxia in the heel-to-knee test. The patient could walk only when supported in a walking machine.

Case 15 (Chart 6).—A man aged 20. The illness had begun about two years previously, with unsteady gait. At the same time the patient's speech became slow and staccato. The symptoms waned for a short time but soon flared up again. On the whole the condition thereafter worsened, especially in the course of the six months before admission to the hospital. On admission, he was of indifferent mood and mentally of somewhat reduced capacity. There was nystagmus on looking to the right and to the left. Ophthalmoscopy showed no definite optic atrophy. There was slightly increased tonus of the upper limbs, with relatively brisk and equal reflexes. There was some terminal uncertainty in the finger-to-nose test, and, in addition, there was dysdiadokokinesia. There was marked spastic increase of tonus in the lower limbs, and the deep reflexes were brisk and equal. The power was diffusely reduced. There was some uncertainty in the heel-to-knee test. The patient could not walk. While he was in the hospital, a periurethral abscess developed (as shown on the curve). However, this resolved in a fortnight.

Case 16 (Chart 7).—A man aged 45. He became ill when he was 28 years old. The first sign of the illness he noticed was the sudden occurrence of loss of power in the lower limbs. The course of the disease has been intermittent, and the condition has gradually worsened. At the start of the investigation the patient was slightly euphoric. There was slight nystagmus on lateral positioning of the eyes. Ophthalmoscopy showed no optic atrophy. On both sides there were slight terminal uncertainty in the finger-to-nose test and some dysdiadokokinesia. The abdominal skin reflexes on the left side were absent. The power in both lower limbs was reduced. The tonus showed marked increase of spasticity, but the deep reflexes were normal. There were a marked ankle clonus and Babinski sign bilaterally. The heel-to-knee test could not be performed at all on the left side and was extremely uncertain on the right. The patient could walk only in the parallel bars.

Case 17 (Chart 8).—A man aged 27. At 18 years of age he developed blurred vision and difficulty in walking. The latter cleared up rapidly, but the blurred vision continued for several months. Four years later difficulty in walking recurred, and after this the condition deteriorated rapidly, in the

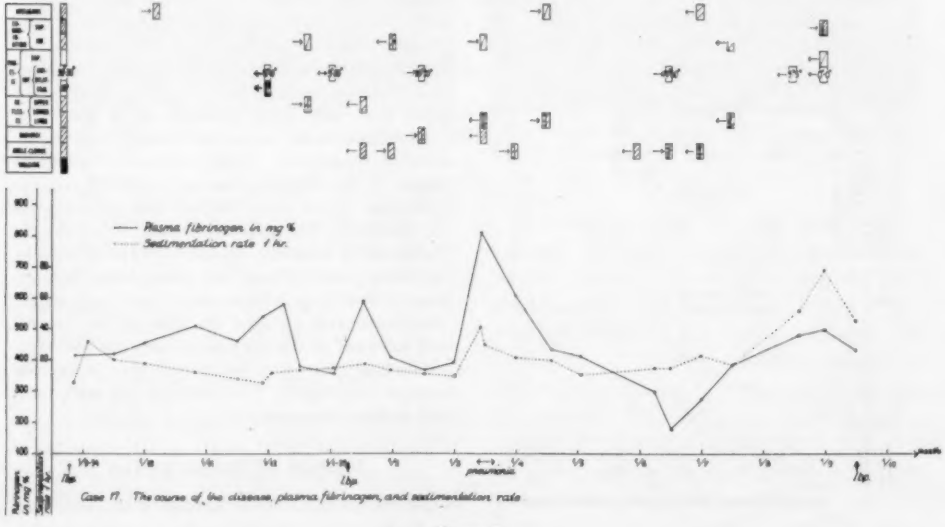


Case 16 The course of the disease, plasma fibrinogen, and sedimentation rate

Chart 7

course of 12 months. On admission he was somewhat euphoric. There was gross nystagmus on looking laterally. Ophthalmoscopic examination showed bilateral temporal pallor. There was some spastic increase of tone in the upper limbs; the reflexes were relatively brisk and equal on the two sides. There was marked uncertainty in the finger-to-nose test. Moreover, there were dysdiadokokinesia and dysmetria. The abdominal reflexes were absent. There was spastic increase of tone in the lower limbs, and the power was diffusely reduced. The deep reflexes were brisk and equal on the two sides. There was a marked bilateral foot clonus and Babinski sign. There was some uncertainty in the heel-to-knee test. The patient was unable to walk.

CASE 18 (Chart 9).—A man aged 48. The illness had started four years before with pain and loss of power in the left upper limb and disturbance of



Case 17 The course of the disease, plasma fibrinogen, and sedimentation rate

Chart 8

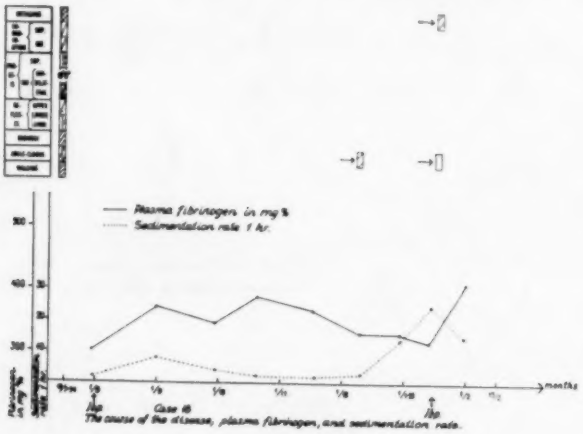

Plasma fibrinogen in mg %
Sedimentation rate 1 hr.
months
Case 18
The course of the disease, plasma fibrinogen, and sedimentation rate.

Chart 9

gait. At the end of a month these symptoms disappeared, but symptoms recurred about six months later. Since then the condition has on the whole deteriorated in that there have been alternative exacerbations and remissions. He was not euphoric but markedly apathetic. There was no nystagmus on looking forward but gross nystagmus on looking in all other directions. Ophthalmoscopic examination showed temporal pallor in the right eye. There was slight spastic increase of tone in the upper limbs. Power was somewhat reduced on the left side. The deep reflexes were rather brisk and equal on the two sides. There was slight uncertainty in the finger-to-nose test. The abdominal reflexes were absent. Power in the lower limbs was diffusely reduced, especially on the left side. The deep reflexes were moderately brisk, with slight preponderance to the left. Babinski's sign was present on both sides, and there was moderate foot clonus with some preponderance on the left side. There was hyperesthesia on the left shin and over the dorsum of the foot. The patient could walk only in a walking apparatus.

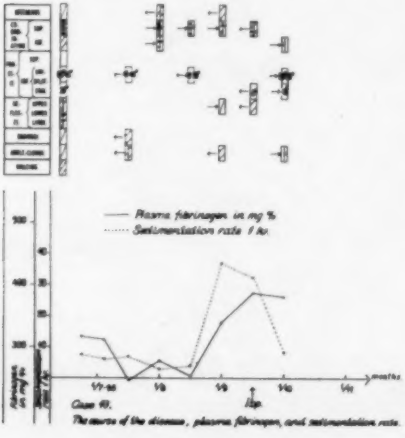


Chart 10

Case 19 (Chart 10).—A man aged 45. Six years prior to admission there developed blurred vision and decreasing vision in both eyes. The symptoms disappeared after six weeks. About six months later there was a relatively sudden loss of power in the left lower limb, but the power gradually returned in the following months. A year later difficulty in walking and slight sphincter disturbances developed. Since then there has been constantly increasing difficulty in walking and new symptoms have developed. The patient was slightly euphoric and erethismic. There was slight nystagmus at the extreme positions of the eyes. Ophthalmoscopic examination showed no optic atrophy or periphlebitis. There was spastic increase of tone in the right upper limb; only slight spasticity in the left. The deep reflexes were moderately brisk, with right-sided preponderance. There was violent intention tremor in the finger-to-nose test, especially on the right side. There were bilateral dysdiadokokinesia and dysmetria. The abdominal reflexes were absent. There was a moderate spastic increase of tone in the lower limbs. There was some diffuse loss of power. The deep reflexes were brisk and equal. The plantar reflex caused spreading of the toes on both sides but no dorsiflexion of the great toe. The heel-to-knee test was performed with a certain terminal uncertainty. The patient could walk only in a walking apparatus.

Method of Investigation

At the same time as lumbar puncture was performed, the blood platelets were counted

according to the method of Heinild (2 ml. of blood is withdrawn into a record syringe, which has been rinsed in 30% sodium citrate solution. The blood is set aside for sedimentation for approximately two hours, and the cells are then counted in the usual way in the counting chamber). Approximately 5 mm. of cerebrospinal fluid and approximately 5 mm. of blood platelet suspension were drawn up in a capillary tube. The contents were then inverted five times. The thrombocytes were then observed in a counting chamber before and after the addition of cerebrospinal fluid. In order to find out whether agglutination of the thrombocytes might occur on addition of fluid alone because of the currents thus formed, control experiments were carried out. In these, partly isotonic saline, partly 3.8% sodium citrate solution, and partly 3% sodium citrate solution were added, but no agglutination, or, at the most, agglutinates consisting of three to four thrombocytes were observed by this means.

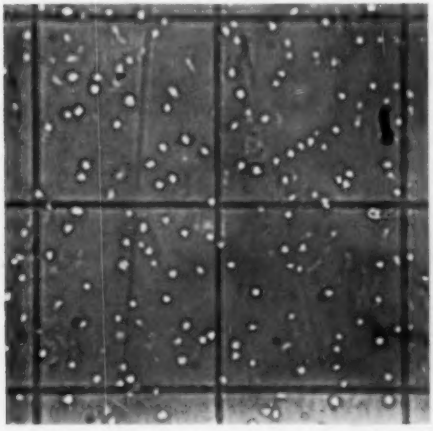


Fig. 1.—Agglutination before the addition of cerebrospinal fluid.

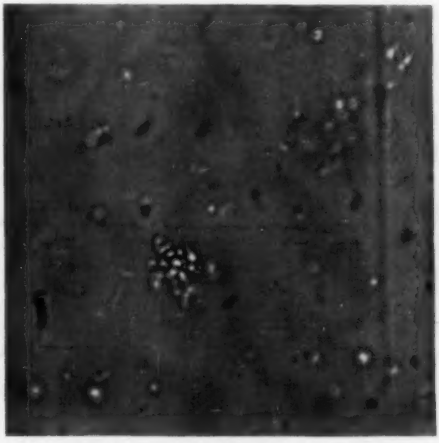


Fig. 2.—Moderate agglutination after the addition of cerebrospinal fluid.

Experimental Results

Before the addition of cerebrospinal fluid there was observed, at most, a slight agglutination of the thrombocytes, with two to three in each agglutinate. The agglutination observed after the addition of cerebrospinal fluid is shown in the accompanying Table.

It can be seen in Figures 1, 2, and 3 how great can be the difference before and after the addition of cerebrospinal fluid.

As shown in the Table, there seems to be a tendency to greater agglutination of the thrombocytes in the phases of progression of the disease, whereas agglutination is not increased, or is increased only to a very slight extent, in remissions or stationary phases. In connection with the exacerbations, the cell count in the cerebrospinal fluid seemed to be somewhat increased; this, however, was sometimes also the case in phases of remission. The total protein content was variable. Moreover, there seemed to be a tendency toward a rise in the plasma fibrin during the phases of progression.

Comment

The investigations described here seem to indicate that in multiple sclerosis a substance is present in the cerebrospinal fluid in connection with the attacks, and that this may contribute to the agglutination of the thrombocytes. In the other phases of the disease this substance seems to be of less importance. Moreover, as a rule, there seemed to be a tendency toward a rise in the cell count in the cerebrospinal fluid in connection with the exacerbations, whereas the total proteins showed a variable state,

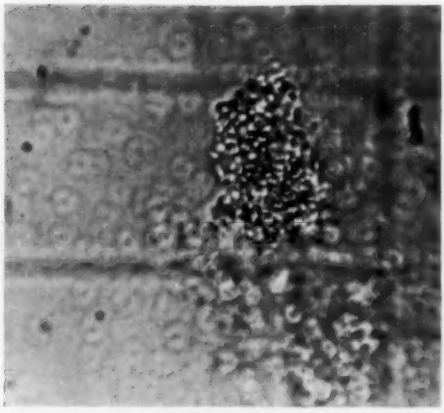


Fig. 3.—Pronounced agglutination after the addition of cerebrospinal fluid.

a finding in agreement with investigations carried out by Freedman and Merritt.[28] In the same way, in agreement with earlier investigations,[29] it was shown that there was a tendency toward a rise in the plasma fibrinogen in connection with the phases of progression.

Since it is thought that in multiple sclerosis the plaques have a tendency to occur at certain sites of predilection, such as the periventricular zones and around the small veins in the central nervous system, the question arises as to whether the thrombocyte-agglutinating substance demonstrated in the cerebrospinal fluid may be considered of importance in connection with this special localization of plaques.

In judging this, the question of the existence and direction of a possible flow of fluid in the perivascular channels in the central nervous system is important. Weed[30] is of the opinion that he has demonstrated the existence of a connection between the subarachnoid space and the perivascular channels of the brain. In normal conditions there should be a flow of fluid along these channels from the brain to the cerebrospinal fluid, and in abnormal conditions in the opposite direction. Sepp[31] postulated that the cerebrospinal blood vessels pumped the cerebrospinal fluid at a great rate into the perivascular channels. Investigations carried out by Schaltenbrand and Bailey[32] and Spatz,[33] on the other hand, gave a diametrically opposite result. The results of the last-mentioned studies can perhaps be explained by the fact that the authors did not use suitable dyes in the investigations. Similarly, also, later investigations carried out by Broman[20] have supported Weed's[30] views. Furthermore, Broman showed that in multiple sclerosis there is permanent disorder in the vascular permeability within the plaques.

The fact that, like the formation of thrombocyte-agglutinating substance, a formation of substance inside the meningeal space may occur is known from investigations carried out by Wallenius.[34] He showed by means of electrophoresis that normally the proteins in the spinal fluid are formed from serum proteins by some kind of filtration process. However, increase in protein in the spinal fluid in other cases, e.g., in multiple sclerosis, may have a pat-

Thrombocyte Agglutination with Cerebrospinal Fluid of Ten Multiple Sclerosis Patients

Patient No.	Date	Cell Count, Cu. Mm.	Protein, Mg/100 Cc.	Approx. No. of Thrombocytes in Agglutinates
Normal		0-5	10-30	0
3	3/27/51	8	27	5
6	8/ 7/52	5	102	5
7	10/15/50	12	17	30-50
8	10/15/50	12	18	100
12	4/13/50	8	22	100
15	8/ 5/54	9	17	50
	1/ 5/55	5	28	0
16	4/23/54	0	27	10-50
	11/29/54	3	34	5
17	8/25/54	10	34	50
	1/ 8/55	12	52	50-100
	9/15/55	5	95	10
18	8/ 1/55	0	31	5
	1/14/55	0	24	0
19	9/15/55	6	31	10-100

tern diverging from that of serum proteins, consisting especially of a rise in γ-globulin. It was his opinion that the cause of this is in all probability a localized synthesis or release of globulin inside the meningeal space.

Thus, in multiple sclerosis it is thought that there occurs a resorption into the small veins of the central nervous system of a spinal fluid which in exacerbations is thought to contain a thrombocyte-agglutinating substance. By this means the commonest type of thrombus, i.e., agglutination of blood platelets,† in multiple sclerosis may be considered to arise. At the same time, this hypothesis seems to offer a reasonable explanation of the periventricular localization of plaques.

Earlier attempts to explain the occurrence of plaques in multiple sclerosis as being brought about by diffuse local thrombosis because of an abnormal clotting mechanism have hitherto been in vain. For one thing, the demonstration of abnormalities in connection with the blood-clotting mechanism has proved possible only by means of highly artificial methods,‡ so that the validity of the experiments is impaired. It has also been difficult to explain the fact that symptoms arise in the central nervous system only, and not in other organs, if an abnormal clotting mechanism is present. It is true that Putnam [14] showed the presence of thrombi in organs other than the central nervous system, and the special structure of these venous plexuses in the central nervous system [19] could mean that in no other site in the organism could a little thrombus cause such serious symptoms.

A looser explanation of the fact that plaques occur at the aforementioned sites of predilection seems to be reached through the supposition that there is an interaction between the thrombocytes in the small veins of the central nervous system and the cerebrospinal fluid, which, in connection with periods of exacerbation, contains a thrombocyte-agglutinating substance. At the same time, changes in the blood, such as the rise in the plasma fibrinogen demonstrated, may also play a part in this connection.

† References 14 and 19.

‡ References 35-36.

Summary

In multiple sclerosis plaques seem to occur at certain sites of predilection, that is, around the small veins in the central nervous system and periventricularly. On the basis of Putnam's thrombus theory, 10 patients with multiple sclerosis were investigated to see whether in the cerebrospinal fluid changes could be demonstrated which might explain the localization of plaques. The result of the investigations was that in connection with the periods of progression the cerebrospinal fluid contains a thrombocyte-agglutinating substance. It could be considered a reasonable explanation of why plaques occur at special sites of predilection to presume that the cerebrospinal fluid in periods of progression contains a thrombocyte-agglutinating substance which penetrates into the small veins of the central nervous system. By this means the thrombi, which consist of masses of agglutinated platelets, would arise.

REFERENCES

1. Cruveilhier, J.: L'Atlas d'anatomie pathologique, Paris, J. B. Baillière, 1835-1842.

2. Rindfleisch, E.: Histologisches Detail zu der grauen Degeneration von Gehirn und Rückenmark, Arch. path. Anat. 26:474, 1863.

3. Charcot, J.: Histologie de la sclérose en plaques, Gaz. hôp. 41:557, 1868.

4. Ribbert, H.: Über multiple Sklerose des Gehirns und Rückenmarks, Arch. path. Anat. 90: 243, 1882.

5. Williamson, J.: The Early Pathological Changes in Multiple Sclerosis, M. Chron. 9:373, 1894.

6. Borst, M.: Die multiple Sklerose des Zentralnervensystems, Ergebn. allg. Path. u. path. Anat. 9:67, 1903.

7. Schuster, P., and Bielschowsky, M.: Beitrag zur Pathologie und Histologie der multiplen Sklerose, Ztschr. klin. Med. 34:395, 1898.

8. Strähuber, A.: Über Degenerations- und Proliferationsvorgänge bei multipler Sklerose des Nervensystems, Beitr. path. Anat. u. allg. Path. 33:409, 1903.

9. Siemerling, E., and Raecke, J.: Zur patho-

logischen Anatomie und Pathogenese der multiplen Sklerose, Arch. Psychiat. 48:824, 1911.

10. Dawson, J.: The Histology of Disseminated Sclerosis, Tr. Roy. Soc. Edinburgh 50:517, 1916.

11. Putnam, T.; McKenna, J., and Morrison, L.: Studies in Multiple Sclerosis: The Histogenesis of Experimental Sclerotic Plaques and Their Relation to Multiple Sclerosis, J. A. M. A. 97:1591, 1931.

12. Putnam, T.: Studies in Multiple Sclerosis: "Encephalitis" and Sclerotic Plaques Produced by Venular Obstruction, Arch. Neurol. & Psychiat. 33:929, 1935.

13. Putnam, T.: Evidences of Vascular Occlusion in Multiple Sclerosis and "Encephalomyelitis," Arch. Neurol. & Psychiat. 37:1298, 1937.

14. Putnam, T., and Adler, A.: Vascular Architecture of the Lesions of Multiple Sclerosis, Arch. Neurol. & Psychiat. 38:1, 1937.

15. Putnam, T., and Alexander, L.: Disseminated Encephalomyelitis: A Histologic Syndrome Associated with Thrombosis of Small Cerebral Vessels, Arch. Neurol. & Psychiat. 41:1087, 1939.

16. Zimmerman, H., and Netsky, M.: The Pathology of Multiple Sclerosis, A. Res. Nerv. & Ment. Dis., Proc. (1948) 28:271, 1950.

17. Macchi, G.: The Pathology of the Blood Vessels in Multiple Sclerosis, J. Neuropath. 13:378, 1954.

18. Dow, R., and Berglund, G.: Vascular Pattern of Lesions of Multiple Sclerosis, Arch. Neurol. & Psychiat. 47:1, 1942.

19. Fog, T.: The Pathological Anatomy of the Spinal Cord in Disseminated Sclerosis, Copenhagen, Ejnar Munksgaards Forlag, 1948.

20. Broman, T.: The Permeability of the Cerebrospinal Vessels in Normal and Pathological Conditions, Copenhagen, Ejnar Munksgaards, Forlag, 1949.

21. Charcot, J.: Des scléroses de la moelle épinière, Gaz. hôp. 41:409, 1868.

22. Westphal, A.: Über Encephalomyelitis disseminata und arteriosclerotische Erkrankungen des Zentralnervensystems in ihren Beziehungen zur multipler Sklerose, Neurol. Centralbl. 28:547, 1909.

23. Lhermitte, J., and Guccione, A.: De quelques Symptomes et lésions rares dans la sclérose en plaques, Encéphale 5:257, 1910.

24. Merle, P., and Pastine, C.: Lésions épendymaires et sous-épendymaires dans la sclérose en plaques, Nouv. iconog. Salpêtrière 23:613, 1910.

25. Schob, F.: Ein Beitrag zur pathologische Anatomie der multiplen Sklerose, Monatsschr. Psychiat. 22:62, 1907.

26. Steiner, G.: Krankheitserreger und Gewebsbefund bei multipler Sklerose, Ergebn. Hyg. Bakt. 12:268, 1931.

27. Hallervorden, J.: Die zentralen Entmarkungskrankheiten, Deutsche Ztschr. Nervenh. 150: 201, 1940.

28. Freedman, D., and Merritt, H.: The Cerebrospinal Fluid in Multiple Sclerosis, A. Res. Nerv. & Ment. Dis., Proc. (1948) 28:428, 1950.

29. Persson, I.: Variations in Plasma Fibrinogen During the Course of Disseminated Sclerosis, A. M. A. Arch. Neurol. & Psychiat. 74:17, 1955.

30. Weed, L.: Studies on Cerebro-Spinal Fluid: II. The Theories of Drainage of the Cerebro-Spinal Fluid with an Analysis of the Methods of Investigation, J. M. Res. 26:21, 1914.

31. Sepp, E.: Die Dynamik der Blutzirkulation im Gehirn, Berlin, Springer-Verlag, 1928.

32. Schaltenbrand, G., and Bailey, P.: Die perivaskuläre Piagliamembran des Gehirns, J. Psychol. u. Neurol. 35:199, 1928.

33. Spatz, H.: Die Bedeutung der vitalen Färbung für die Lehre vom Stoffaustausch zwischen dem Zentralnervensystem und dem übrigen Körper, Arch. Psychiat. 101:276, 1933.

34. Wallenius, G.: Electrophoretic Patterns of Cerebrospinal Fluid and Serum Compared in Normal and Pathological Conditions, Acta Soc. med. upsalien. 57:138, 1952.

35. Simon, B., and Solomon, P.: Multiple Sclerosis: Effect of Typhoid Vaccine and of Epinephrine on Coagulation of the Blood, Arch. Neurol. & Psychiat. 34:1286, 1935.

36. Simon, B.: Blood Coagulation in Disseminated Sclerosis and Other Diseases of Brain Stem and Cord, Arch. Neurol. & Psychiat. 48:509, 1942.

Hemochromatotic Pigmentation of the Central Nervous System

A Clinicopathologic Study

META A. NEUMANN, M.S., Washington, D. C.

In 1942 Lewey and Govons [1] reported a case of hemochromatotic pigmentation of the central nervous system. Their patient showed progressive deafness and difficulty in walking, but had not evidenced any of the clinical signs of classical hemochromatosis or other visceral disturbance. For this reason, the autopsy was restricted to the head. The neurologic symptoms had persisted over a six-year period. In 1948 a similar case was recognized,[2] in which almost identical clinical disabilities had progressed over an interval of 16 years. The deposition of hemosiderin and hemofuscin was identical in distribution to the first-described case, namely, in peripheral zones of cortex and brain stem and periventricular regions, with especially severe involvement of the cerebellum, where crests of many folia had undergone extensive necrosis. Perusal of an article by Noetzel,[3] in which a similar distribution of iron pigment was attributed to old subarachnoid hemorrhage, was of interest, since both of his patients had evinced difficulty in gait, and one disturbance of hearing. The remarkable resemblance of clinical and pathologic findings in these four cases led to the hypothesis that a new syndrome had been established. No pigmentation of the viscera was reported in Noetzel's study, but in Neumann's case the liver cells showed both types of pigment; there was also some pigment in the serosa of other visceral organs. Bronzing of the skin had not been observed during the hospitalization of the patient; neither did he suffer from diabetes or hepatic cirrhosis.

Another clear-cut instance of this condition has now been studied in detail. It is therefore deemed of some importance to record the findings and state again why this picture must be separated from the usual type of hemochromatosis, as well as from other well-known instances of iron deposition in the brain.

Recorded for publication March 8, 1956.

St. Elizabeths Hospital.

Report of a Case

The patient, a white woman of 55, was admitted to St. Elizabeths Hospital on Oct. 7, 1947. Abnormal findings were a marked defect in hearing, hyperactive deep tendon reflexes, and swaying in the Romberg position. The finger-to-nose test was carried out poorly. She was correctly oriented, but claimed her hospitalization was the result of "evil powers" working on her.

The patient was born in Ireland; all immediate ancestors and siblings died there except the informant, a younger sister. One brother died of cerebral hemorrhage; the causes of death of the others were not known. The patient had measles in childhood. She completed the eighth grade of school and came to the United States in 1913, when she was about 20 years of age. She had worked as a domestic until her progressive deafness (onset at about the age of 40) had rendered this occupation untenable. A hearing aid was "too noisy for her head." She did not make friends easily and never married. She drank beer occasionally, but there was no history of intoxication at any time. After she ceased to work, the sister furnished her support. During this period the patient's activities consisted of reading, playing solitaire, and going to church.

About two years prior to hospitalization the patient began to talk "irrationally." On the night of Sept. 26, 1947, she was exceptionally disturbed and noisy. This behavior led to her commitment to the District General Hospital for observation. After her admission to St. Elizabeths Hospital she was at first quite assaultive. The formal diagnosis was psychosis with cerebral arteriosclerosis with involutional factors.

The patient appeared tense at the time of a physical examination in May, 1949; her blood

pressure was recorded as 190/98 mm. of mercury. On later occasions it was generally within normal limits. Except for her deafness and arteriosclerotic changes of the retinal vessels, there were no gross neurologic findings. If the examiner raised his voice, she was able to understand and answered all questions promptly, coherently, and relevantly. It was stated that the patient did not speak clearly. About a year later, in February, 1950, symmetrically hyperactive deep tendon reflexes and a bilateral Hoffmann sign were reported. In addition, it was stated that the patient tended to veer toward the right in walking and supported herself by the wall. She cooperated poorly in sensory testing, but seemed more than usually sensitive to pinprick. She also showed transient ankle clonus on both sides and adductor spasm of the legs. There were flexion contractures of the fourth and fifth fingers of both hands.

Numerous falls were reported during the last four years of her hospitalization. They appeared to be the result of her unsteadiness of gait. On Sept. 30, 1953, she sustained an intertrochanteric fracture of the left femur. She proved a difficult nursing problem, and soon numerous decubitus ulcers formed, which were resistant to therapeutic measures. She later developed a urinary infection. The temperature was usually above normal in her final illness, but never rose above 102 F. She died March 23, 1954.

Laboratory Data.—The first two hematologic reports (1948 and early 1951) were within normal limits. In July, 1951, the red cell count had dropped to 3,990,000. It continued to decrease slightly, but was below 3,000,000 only once—2,850,000 on Oct. 24, 1953. The hemoglobin on that date was 67.5%. In October, 1953, a catheterized urine specimen yielded, on culture, a heavy growth of coliform bacilli. Blood chemistry tests and blood and spinal fluid serology were not indicative of pathologic changes.

Necropsy Findings (Autopsy performed 26 hours after death by Dr. A. H. Kiracofe).—Externally, the only significant lesions were the numerous decubitus ulcers. No discolorations of the skin, mucous membranes, or serous linings were noted. It was stated that the aorta and other arteries were amazingly well preserved. The urinary bladder contained three small stones and had a hemorrhagic mucous membrane. Other viscera were apparently healthy, including the liver. The brain showed brownish discoloration over the basilar surface of the cerebellum and medulla oblongata and the basilar surface of the frontal lobes, in the olfactory tracts and bulbs, believed to be the result of subarachnoid bleeding. No other abnormalities were recorded. Death was attributed to the decubitus ulcers, lobar pneumonia of the left lower lobe, and pyelonephritis.

When the brain was examined after fixation, the focal peripheral distribution of the brownish discoloration and the superficial rusty-colored softening of certain cerebellar folia, coupled with the long-standing impairment of hearing and progressive unsteadiness of gait, strongly suggested that this was a second case of hemochromatotic pigmentation of the central nervous system, not as advanced as the instance reported in 1948.[2] It was noted now that the pia-arachnoid over the inferior surface of the cerebellum was thin and pale, with no trace of hemosiderin staining, while the underlying parenchyma was definitely a rusty-brown (Fig. 1). This was also the case on the superior surface of the cerebellum in the anterior lobe. A sagittal section through this region showed that the brownish discoloration extended about 8 mm. into the interior. Gradually this discoloration faded into the pale folia of the simple lobule. The rust-colored folia were decreased in consistency. Both flocculi were softened and brown. There was no gross change in the dentate nuclei or central medullary substance of the cerebellum. Peripheral brownish discoloration, about 1 mm. in width, of the midbrain, pons, medulla oblongata, and upper cervical cord was similar to the previously described case of hemochromatotic pigmentation.

Fig. 1.—Undersurface of cerebellum. Note pale transparent leptomeninges and brownish discoloration of paramedian lobules and anterior folia of the ansiform lobule.

On the convex surface of the cerebrum there was no rusty staining of the leptomeninges or parenchyma. On the undersurface the brown discoloration was confined almost entirely to the olfactory bulbs and tracts and did not involve the adjacent gyri recti or other orbital convolutions. The rusty color diminished gradually toward the trigone areas. The hippocampal gyri, particularly the right, also showed brownish discoloration. Minute triangular defects, between 1 and 2 mm. in size, were observed in the right

second and third temporal convolutions; they were pale yellowish-brown and constituted the only recognizable traumatic lesions in this brain. On cross section, it was noted that the entire cut surface of the olfactory tract was dark brown and that the adjacent brain tissue was of normal hue. There were similar discoloration on the posterior border of the splenium of the corpus callosum and traces of rust color superficially in some of the temporal convolutions. Ependymal linings were pale.

*Microscopic Examination.**—Viscera: The presence of pyelonephritis, superimposed on chronic glomerulonephritis, was confirmed. The urinary bladder showed a hemorrhagic cystitis. There was terminal congestion of the heart, lung, and spleen. Petechial hemorrhages were observed in the myocardium. The pancreas showed fatty infiltration; the thyroid gland, fibrosis. Arteriosclerosis was noted in the ovary and spleen. The adrenal gland was considered normal. The pituitary gland showed focal capsular lymphocytic infiltration.

The hepatic architecture was well preserved, with no trace of cirrhosis. Many of the cells, especially those radiating around the central veins, had fine yellowish-brown granules in their cytoplasm (hematoxylin-eosin, Fig. 2). With the specific techniques employed the majority of the granules took the red color of hemofuscin, although in certain areas groups of granules had the bright blue of iron salts (Perls and Tirmann-Schmeltzer methods gave essentially similar results). Sometimes both types of pigment were present in the same cells or in adjacent cells. Pigment granules were rarely observed in Kupffer cells; these cells were heavily loaded with iron in a classical case of hemochromatosis examined at about the same time.

Blue-stained granules of iron were demonstrated rarely in other visceral sections. They were generally considered artifactual or believed to be hemosiderin from degenerating red cells. The significance of iron-reacting deposits in the ovary was not clear. Rounded concretions of the pineal gland reacted positively for iron; a few of the larger globules had reddish centers. Red granules of hemofuscin were observed in macrophages in the capsule of this gland. Faintly stained reddish granules were also noted in some of the myocardial cells. The pigment in the cells of the pars nervosa of the pituitary gland took the red color of hemofuscin.

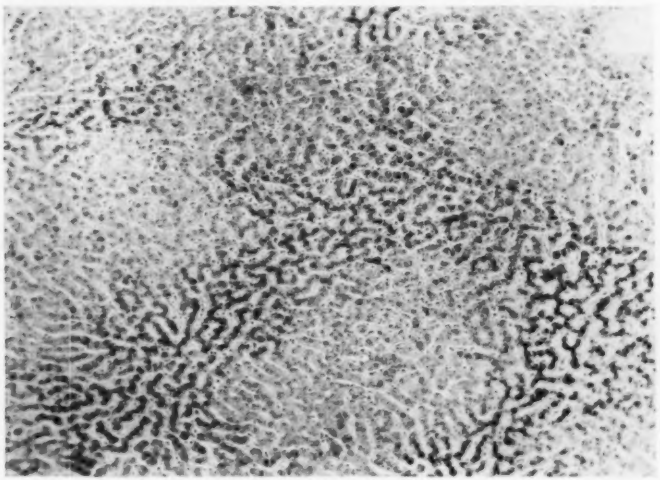


Fig. 2.—Liver, showing focal distribution of pigment granules in hepatic cells. Perls' method, counterstained with Mallory's basic fuchsin; 16 mm. obj.

Central Nervous System: In the areas of gross brownish discoloration the hematoxylin-eosin method showed massive numbers of phagocytes loaded with brown pigment. In addition, fine granules of gray or brown pigment were observed encrusting processes of astrocytes, and less frequently of microglia cells. With specific techniques the brown deposits reacted positively for iron; the grayish granules showed the red color

* All visceral and brain sections were stained by hematoxylin-eosin and the Perls and Tirmann-Schmeltzer methods for ferric and ferrous iron, with counterstaining with Mallory's basic fuchsin for hemofuscin in both.[4] The cerebral sections were also studied by means of the Weil, Holzer, and Davenport techniques. The oil red O method for fat, the Ziehl-Neelsen acid-fast technique, and the Braunmühl stain were carried out on certain brain sections. The alizarin red S method for calcium also was employed.

of hemofuscin. Many free globules of iron were deep blue in color; there were also slightly larger, pale-blue globules which appeared to be gitter cells, although nuclei were not always visible. In some areas, chiefly in the cord and medulla oblongata, the peripheral phagocytes had a pale rose-red tinge; the small granules of hemofuscin were always of a deeper red tone. No calcium was demonstrable in the deposits. Holzer stain showed marked reactive gliosis wherever the pigmentation was most intense, as in margins of the brain stem and spinal cord and in the cerebellum. The hemofuscin was scarcely visible in the Weil, Holzer, and Davenport techniques, or a very pale gray; iron remained brown. Nerve cells were free from pigment except in rare instances.

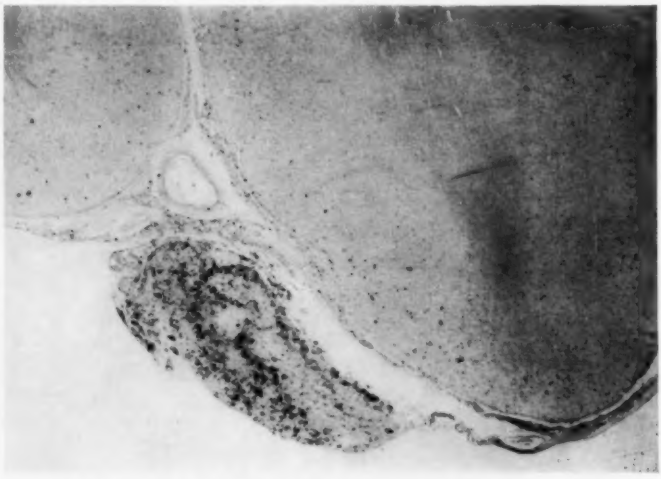


Fig. 3.—Left orbital region, showing marked accumulation of deposits in olfactory bulb and scattered pigmentation of adjacent areas. Perls-Mallory technique; reduced to 3/5 of mag. × 20.

The section from the left orbital region showed central loss of myelin and reactive gliosis in the olfactory bulb, where there was a heavy deposition of iron-reacting pigment but very little hemofuscin (Fig. 3). Pigment-laden phagocytes were scattered in the adjacent pia-arachnoid, rapidly diminishing in quantity in distant areas. In the molecular layer, iron deposits and hemofuscin granules encrusted processes of astrocytes. Because of the high incidence of iron deposition in the rostral portion of the olfactory tract, a section was taken from the grossly paler trigone area. There was no significant pigmentation among the olfactory fibers. Iron-reacting globules were thickly clustered in the peripheral zones and even in deeper areas, generally around blood vessels; fine granules of both types dotted glial processes. This spread of deposits into deeper layers was rarely observed in other cortical areas. The medial olfactory striae were included in a section from the posterior part of the right frontal lobe; they were free from pigment. There were likewise no deposits on the dorsal surface of the superior frontal convolution, but a few globules and granules were noted superficially along its medial surface, in the cingular cortex, and in the overlying pia-arachnoid.

In a section from the splenium of the corpus callosum iron-reacting globules were thickly clustered on and near one surface; a few were also demonstrated in the marginal layer of the fasciola cinerea. Globules which reacted positively for iron and were about the size of a well-filled gitter cell were numerous in the molecular layer of the uncus and hippocampal gyrus. There were also some in the second layer, but not deeper. As in other areas, the marginal glia cells were encrusted with both types of granules. The hippocampus was free from pigmentation.

The right temporal lobe section included the small, obviously traumatic, scars. Iron deposits were present in the vicinity of the lesions; hemofuscin granules encrusted small astrocytes of the molecular layer and were engulfed in gitter cells in perivascular spaces in the white matter. A few "calcified" nerve cells near the defects reacted for ferric salts (Perls' reaction) but not for ferrous salts or calcium.

Iron deposits were demonstrated on the ventral surface of the mammillary body, cerebral peduncle, and optic tract. There was fibrillary gliosis in the areas of pigmentation and throughout the visual path in this series of sections.

In another subcortical section there was loss of myelin in the medial aspect of the pulvinar. Deposits were thickly dispersed throughout this region; many were perivascular in distribution. The nerve cells of this area had grayish-yellow

cytoplasm, interpreted as lipofuscin, in the hematoxylin-eosin stain. With Mallory's method for hemofuscin, this portion of the cell body was filled with bright-red granules; these were acid-fast in the Ziehl-Neelsen technique. The Holzer stain demonstrated intense gliosis in the region of iron deposits and mild hyperplasia of astrocytes in other thalamic areas.

Iron deposits in the tectum formed a layer 1 mm. in width, corresponding to the grossly visible brown rim (Fig. 4*A*). The pigments were numerous in the thick glial band in all peripheral zones of the pontomesencephalic sections (Fig. 4*B*), including the interpeduncular fossa. A small number of iron globules were scattered among the pontine nuclei. The pigmented nerve cells of the substantia nigra did not react positively for iron. There was very little free pigment in the pia-arachnoid in spite of the heavy peripheral distribution. Hemofuscin granules were in the walls of, or near, pial and parenchymal blood vessels. There was loss of myelinated fibers in the tectum, and the crossing fibers between the inferior colliculi, as well as the fibers in the brachia of these structures, were greatly reduced in number. Elsewhere myelination was well preserved. Many of the nerve cells of the tegmentum showed central chromatolysis. One binucleated cell was observed.

Sagittal sections from the anterior lobe of the cerebellum showed small cystic defects at the crests of several folia. The molecular layer was greatly narrowed adjacent to the defects and

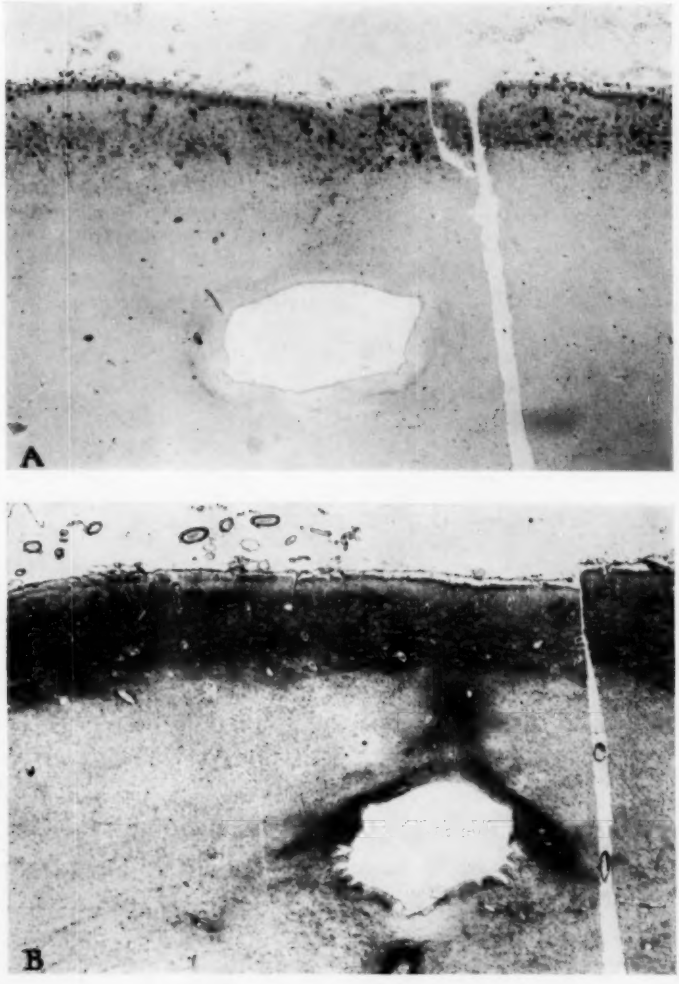


Fig. 4.—Tectum. *A*, iron deposits near surface. Perls' technique; reduced to 3/5 of mag. × 20. *B*, fibrillary gliosis in area of iron and hemofuscin pigmentation. Holzer stain; reduced to 3/5 of mag. × 20.

showed intense fibrillary gliosis, but almost no iron deposits. All of the folia were atrophic; related to the atrophy was a widespread deposition of pigment. The majority of the Purkinje cells had disappeared in the most severely degenerated leaflets. Granules of hemofuscin and iron, closely intermingled, encrusted the processes of the hyperplastic Bergmann's glia (Fig. 5). Larger globules of iron were also observed in this layer. There was very little pigment in the granule layer, except in the most damaged folia, where these cells had also disappeared. On the other hand, the central cores of white matter showed myelin loss, reactive astrocytosis, and many deposits. This was very striking in the folia of the superior portion of the anterior lobe and near the crests of its posterior folia, and also in the crests of the leaflets of the simple lobule and in the nodule of the vermis. Over the culmen there was an area of focal fibrosis of the pia-arachnoid, which contained a few iron concretions.

Interrupted serial sections were prepared from the upper level of the medulla oblongata and cerebellum. There were extensive iron deposits in the flocculus and its peduncle and adjacent cerebellar folia. It should perhaps be emphasized that the pigment was not uniformly distributed in the cerebellar folia. The flocculus and anterior lobe were most involved; the vermis and paramedian lobules, less so, and the ansiform lobule contained almost no pigment. The distribution of the pigments within the folia was similar to that in the an-

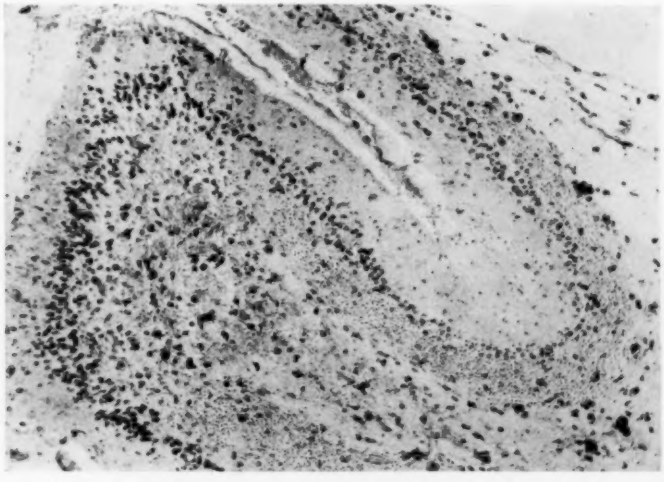


Fig. 5.—Cerebellum, in an area showing total loss of Purkinje cells and focal loss of granule cells. Iron and hemofuscin deposits, most intense in layer of Bergmann's glia. Perls' reaction, counterstained with basic fuchsin; 16 mm. obj.

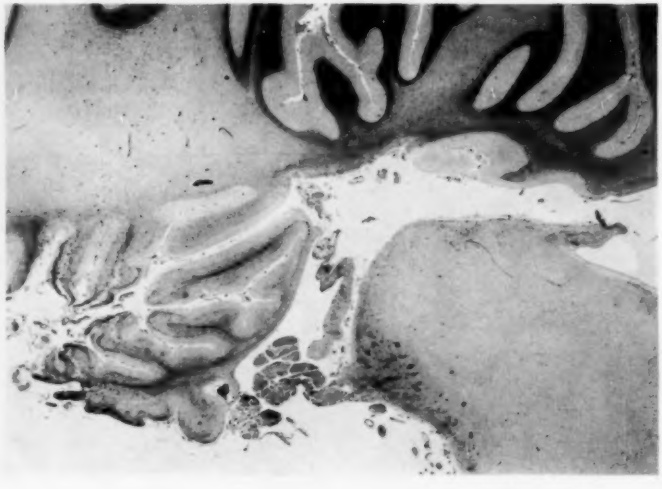


Fig. 6.—Region surrounding the foramen of Luschka, showing distribution of pigments. Perls-Mallory stain; 64 mm. Summar.

terior lobe. As noted in Figure 6, small defects had also occurred at the crests of some of the folia of the flocculus. The molecular layer showed considerable variation in width; the amount of reactive fibrillary gliosis was in direct proportion to the damage. Myelin loss was present only where much pigmentation had occurred. There was no pigment in the dentate nucleus in most sections of the series. At some levels occasional granules of iron were observed; hemofuscin was somewhat more abundant. The nerve cells of the dentate nucleus contained increased lipofuscin pigment. There were moderate proliferation of microglia and oligodendroglia in this nucleus and astrocyte hyperplasia throughout the medullary substance.

In the medulla, pigmentation and gliosis were prominent in peripheral zones and absent in central areas (Fig. 6). The large globules reacted for iron; hemofuscin granules were prominent in swollen macrophages of the thick marginal glial band. There was extensive pigmentation of both types among the root fibers of the eighth and ninth nerves (Fig. 7). Loss of nerve fibers was demonstrable in involved nerves; the remaining sheaths and fibers of these nerves showed degenerative changes. There was moderate loss of nerve cells in the lateral and medial vestibular and ventral cochlear nuclei; the dorsal cochlear nuclei seemed less involved. Many of the remaining nerve cells were pyknotic. Pigmentation was not intense in any of the nuclei of the eighth nerves. Fibrillary gliosis and microglial proliferation were present only where there was loss of neuronal elements. A few thin bundles of myelin sheaths showing degenerative changes passed dorsal to the restiform body in a thick glial band; they appeared to be cochlear fibers. In the restiform body pigment was only present peripherally.

In a lower level of the bulb there was similar peripheral distribution of iron and hemofuscin. The Holzer preparation strikingly demonstrated the thick glial meshwork of the margin, in the floor and taenia of the fourth ventricle and in the raphe and inferior olives. There was slight extension of the glial proliferation in the spinal vestibular nuclei and lateral reticular substance, where some of the nerve cells showed central chromatolysis. A vessel in one dorsal motor nucleus of the vagus had a wide collar of lymphocytes. This was the only perivascular infiltration observed in the numerous sections.

In the upper cervical cord there was myelin loss in the columns of Goll, almost complete in the peripheral areas. There was also slight loss of myelin in other marginal regions, particularly the zones of Lissauer. The Holzer stain demonstrated reactive gliosis in these areas, in the ventral horns, and around the central canal. Hemofuscin was in the form of fine granules in phagocytes of the thick peripheral glial meshwork. Granules of iron were scattered rather sparsely in demyelinated areas.

In the leptomeninges fine granules of both types, or globules of iron, were generally present only in areas where there was underlying pigmentation of the parenchyma. Granules of iron and hemofuscin were observed in the walls of numerous blood vessels in the subarachnoid space, with hemofuscin somewhat more prominent. In the spinal cord and medulla oblongata sections, the pia-arachnoid was moderately fibrosed.

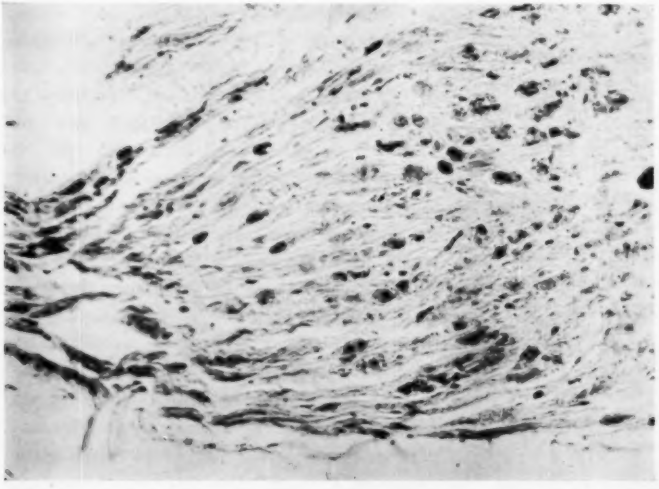


Fig. 7.—Pigment granules, free and in macrophages, among the root fibers of the eighth nerve (glial portion). Perls-Mallory technique; 8 mm. obj.

As to ventricular surfaces, deposits were exceedingly rare. One globule of iron was observed in the ependyma of the inferior horn. A few granules were in the wall of the third ventricle. There were none in the lining of the aqueduct or the floor of the fourth ventricle. A few shallow granulations were occasionally observed on ependymal surfaces.

The choroid plexus adjacent to the epiphysis took the bright-blue color of iron salts. This reaction was not present in the choroid epithelium of the posterior horn. In the fourth ventricle only a few epithelial cells of the choroid contained iron pigment. Laminated concretions in the lateral recesses reacted for iron but not for calcium. The taenia of the fourth ventricle contained much pigment.

The alizarin S method did not demonstrate calcium in any of the deposits. The oil red O-pyridine stain for fat also failed to show any lipoid deposits. The Ziehl-Neelsen reaction showed acid-fast granules in some of the nerve cells; this was especially prominent in the posterior thalamus.

Amyloid bodies were present focally in the thick marginal feltwork. They did not react for iron or hemofuscin.

In both the patients at St. Elizabeths Hospital there were progressive deafness and gait disturbances of gradual onset. Deafness was present for 16 and 20 years, respectively, in the two patients. This is of interest in view of the apparently only moderate damage to acoustic pathways in the reported case. Noad and Haymaker [5] also found what they considered insufficient changes in the glial portions of the cochlear nerves and nuclei to account for the deafness which was often a concomitant of tsutsugamushi fever. The glial portion is unusually long in this nerve, and, according to Courville,[6] is the most likely part to be affected by injury or toxic agents. In the presented case there was less pigmentation in the short portions of the peripheral nerves included in the sections than in the glial parts, and since there was definite reduction of nerve fibers in the entering roots, it is believed that the patient's diminished auditory acuity may be attributed to these defects.

Noad and Haymaker also noted pathologic changes in other cranial nerves, but none of their patients exhibited symptoms referable to these disturbed structures. Similarly, in the reported case, there was no clinical evidence of glossopharyngeal dysfunction, although there were much pigment among the root fibers and some diminution in their number. Olfactory function was apparently not tested.

The gait disturbances were obviously related to structural changes in the cerebellar and vestibular pathways. The fact that the patient showed progression of her symptoms indicates that the deposition of pigments was a continuing process.

At the time sections from the second case at this hospital were being prepared, a case of classical hemochromatosis came to autopsy. Sections from the organs of both patients could thus be stained by similar techniques and compared in great detail. In the patient with bronze diabetes there was no pigmentation in any areas of the brain or in the choroid epithelium.

Sheldon, who has done the most searching analysis of hemochromatosis,† stated that one or more of the well-known triad of symptoms may be absent. Deposits are seldom found in brain tissue proper, but have frequently been observed in the choroid plexus, pituitary and pineal glands, and leptomeninges. In his text he cites two instances in which the olfactory bulbs and tracts were pigmented (cases of Hess and Zurhelle, and Wegener), but not the brain stem and cerebellum. In Wegener's case [9] there was also rusty discoloration of the ependymal surfaces of the lateral ventricles and of the choroid plexus. The skin and practically all of the viscera showed marked pigmentation. The microscopic findings in the brain were not discussed in this article.

In the case described in this study, and the one discussed in 1948,[2] iron and hemofuscin pigments were found in the central nervous system *and* liver. The granules were chiefly in hepatic parenchymal cells; there was no cirrhosis. No deepening in color of the organ was described at the autopsies (not seen in the fresh state by me), but certainly after

† References 7 and 8.

the tissues were reexamined, after prolonged fixation in formalin, the dark-brown appearance of the preserved specimens was strikingly different from that observed in normal livers after an equally long fixing period. In the earlier study, pigment granules were found in serosal surfaces of the kidney, adrenal, and pancreas, but no pigment was demonstrated in these organs.

McDougal and Adams [10] reviewed a series of cases of classical hemochromatosis. Many of them showed pigments of both types in the choroid plexus; hemosiderin was demonstrated in the area postrema, pituitary gland and adjacent tuber cinereum, subfornical body, and blood vessel walls of the lenticular and dentate nuclei. This distribution was not found uniformly in all of their 18 cases; none showed a distribution such as that described in this study. In their published abstract they refer specifically to the cases reported by Lewey and Govons, and Neumann; but, since they have never observed an identical case, their conclusion seemed unjustified when they stated: "From the pathologic findings it is concluded that hemosiderin and hemofuscin in brain tissues and meninges can result from hemorrhage alone, and that in the absence of pigment cirrhosis and pigmentation of other viscera the diagnosis of hemochromatosis is not justified. Furthermore in proven hemochromatosis these pigments are largely confined to parts of the brain that have secretory or gland-like function." They also state: "Inasmuch as these same pigments may be found in any hemorrhage, their presence in a single organ does not constitute a sufficient criterion for hemochromatosis." In my own experience, with specific techniques, I have generally been able to demonstrate only hemosiderin, and not hemofuscin, in cases of cerebral bleeding. Many cases showing residuals of hemorrhage either in subarachnoid space or intracerebrally have come under personal observation; yet in none of these cases has the particular type of pigment distribution described been observed. Furthermore, in old intracerebral hemorrhages, the resultant hemosiderin formation clearly remains confined to the environs of the blood extravasations; the macrophages with engulfed pigment do not migrate to distant areas. It should be emphasized that in the reported case the pia-arachnoid was pale and transparent over the cerebellum where the underlying parenchyma was a deep rusty-brown.

Cammermeyer [11] also believed that the pigmentation described by Lewey and Govons and by Noetzel was the result of intrameningeal hemorrhage. He demonstrated iron in paraventricular areas in cases of classical hemochromatosis. In his article he refers briefly to an early patient who showed no clinical evidence of hemochromatosis; the brain, however, showed brownish discoloration of the leptomeninges, and much hemosiderin pigment microscopically, even in the cerebral cortex and olfactory tract. He attributed the massive pigmentation to intrameningeal hemorrhages, since his patient had a vertebral artery aneurysm. It seems possible that this case could fall into the category described in this presentation.

It would be difficult to reconcile the sites of pigment distribution with the possible occurrence of leptomeningeal bleeding. It is also difficult to believe that continuous or recurring small hemorrhages would progress over such a long span of years; if a massive hemorrhage had occurred, the patients would undoubtedly have shown clinical symptoms of sudden onset. This, however, was not so, except in one of Noetzel's patients. The other five recorded instances showed an insidious course over a period of years. Nevertheless, Noetzel appears convinced that the pigments, which had a distribution in his patients similar to that in the cases of Lewey and Govons, and Neumann, were derived from old hemorrhages. In his third case he described traces of hemosiderin in liver cells.[12]

The only possible source of red-cell extravasation in the reported case were the two minute lacerations in the right tem-

poral lobe. They could, under no circumstances, have been responsible for the massive distribution of iron and hemofuscin as demonstrated in the brain. Much more extensive examples of old trauma, accompanied by hemorrhage and laceration of superficial cerebral areas, have frequently been observed in the routine examination of brains at St. Elizabeths Hospital. None of these have exhibited gross peripheral brown discoloration at sites distant from the lesions. In the traumatic lesions personally studied, fine granules of hemosiderin may be observed on processes of small astrocytes in the molecular layer only near the lacerations. Red-stained granules of hemofuscin have not been noted near such defects.

The focal damage to crests of cerebellar folia does not appear to be on a traumatic basis from the location of the defects—in the flocculi, vermis, and anterior lobe. This focal necrosis is probably an early stage of the much more extensive destruction which had occurred in the first reported case, where the entire anterior lobe was destroyed.[2] The fibrillary gliosis of the molecular layer, absence of Purkinje cells and proliferation of Bergmann's glia, moderate loss of granule cells, and astrocytosis of the central cores of the folia are similar to the changes manifested in sclerotic atrophy of the cerebellum, with the exception of the pigmentation.

The reasons for dismissing extravasated blood as the source of the pigments was discussed in my previous study;[2] the present case strengthens this conviction. Sheldon, in his detailed monograph, definitely ruled out products of red cell degeneration as concerned in the formation of the pigments in patients manifesting bronze diabetes. Other investigators also believe that classical hemochromatosis is not the result of excessive hemolysis.‡ There appears, then, to be no valid reason for assigning the deposition of identical pigments in the central nervous system to blood extravasations.

‡ References 13 and 14.

Finally, the work of Hammes[15] on the reaction of the meninges to blood indicates that the onset of hemorrhage is dramatic in nearly every case. The ultimate disposal of the iron pigment, which appears first on about the third day, is not described. However, in his cases of long survival, he states that the only evidence of old hemorrhage is a patchy fibrosis, which has a tendency to obliterate the subarachnoid space.

Since hemosiderin is a blood derivative, it would seem more accurate to refer to the major pigment of hemochromatosis and hemochromatotic pigmentation of the central nervous system as iron, since it is probably inorganic in nature and has never been proved to originate in red cells. Strassman[16] clearly recognized that the iron frequently observed in the basal ganglia is not the result of hemorrhage. In discussing the occurrence of this tissue iron, he pointed out that the iron compounds react to specific stains as hemosiderin derived from red cells, but its origin and significance are still in doubt.

Pearse[17] has discussed the histochemistry of various pigments but advances no theory as to the origin of inorganic iron and calcium in tissues. The nature of hemofuscin is not definitely established. He states that there is not sufficient histochemical evidence to permit retention of a separate fuscin pigment derived from red cells, under the title hemofuscin. He discusses its probable relation to the lipofuscins, since it reacts similarly, and to certain acid-fast pigments, which are sometimes demonstrated in the central nervous system. Since hemofuscin is apparently related to this acid-fast pigment demonstrated occasionally in nerve cells, and to the pigment found in heart muscle in cases of brown atrophy, surely it must have some origin other than from red cells.

The cerebrospinal fluid must next be considered as a possible source of derivation of the pigments. This seemed the most likely origin in the first-described instance at this hospital. This theory was based on

the heavy peripheral and periventricular distribution of the deposits, together with the extensive infiltration of pia-arachnoid with iron-filled macrophages, which resulted in deep-brown staining of the membranes. In the present instance there was much less involvement of the leptomeninges and none of the ependyma. Only the choroid epithelium near the pineal gland contained iron pigment. Ordinarily the pia-glia membrane might act as an effective barrier to the passage of large particles from the circulating fluid into the cerebral parenchyma. A blood-fluid barrier was postulated by Goldman and later Spatz,§ when a dye injected into cerebrospinal fluid diffused into marginal zones of cerebral tissue to walls of vessels. Spatz [18] had also noted that India ink injected into the subarachnoid space merely accumulated in the space, arrested at the pia, without penetrating the subarachnoid processes around vessels entering the cerebral tissue. This experimental evidence of nonpassage of colloidal particles into brain tissue received nice confirmation during the study of the brain of a patient who had undergone a prefrontal lobotomy 17 years before death. At the time of the surgery Thorotrast was injected at the operative site to outline the lesion. Autopsy showed that the leptomeninges were diffusely thickened and had a peculiar uniform silvery tinge. Histologic study showed a massive number of Thorotrast-filled macrophages closely packed in the thick, fibrosed pia-arachnoid, but very little in the surgical defects. There was almost no extension of this material into the brain substance, with the exception of granulomas at the ventral border of each putamen; one of these was at the base of a needle tract crossing the corpus striatum. Very rarely a few superficial vessels had collars of Thorotrast-filled gitter cells. The marginal glial meshwork was thickened.

In the patients with hemochromatotic pigmentation of the central nervous system the deposition of pigments in peripheral zones might argue for a poorly functioning brain barrier, if such exists. It seems to me, however, that if the pigments were the result of absorption from the circulating fluid, the distribution would be more uniform. Granted that in the brain stem such is generally the case, the focal distribution in other areas seems to belie this. For example, on this basis it would be difficult to explain the heavy iron accumulations in the olfactory bulbs and tracts. Iron deposits were scattered in the pia-arachnoid of the cerebellum, but were not nearly as numerous as in the degenerated folia; similar conditions prevailed in other areas of cerebral pigmentation. The presence of deposits in the central cores of the folia, particularly the marked involvement of the Purkinje layer, and scanty deposits among the intervening granule cells, also appear to negate the theory of absorption from the cerebrospinal fluid. One would expect more deposition in the choroid plexus if such were the case; but this has not been demonstrated, although in classical hemochromatosis the choroid epithelium is often loaded with iron. Sheldon stated that there is no information to the effect of the pigment on the composition of the cerebrospinal fluid. To confirm a theory of the derivation of the iron and hemofuscin from the fluid, chemical tests for the presence of these substances would have to be carried out. As far as is known, this has not been done; Sheldon, however, carried out chemical analyses of the tissues of patients with known hemochromatosis and found that iron was increased in the tissues, but decreased in the blood. This was also true in two cases in which the iron content of the brain was analyzed.[8] He found the amount of iron varied somewhat in different areas.

A third possibility to be considered for the derivation of the pigments is a disorder of metabolism resulting in deposition of iron and hemofuscin in situ. Selective deposition of iron and/or calcium in the brain is, of course, not a new or rare phenomenon. But the particular distribution discussed in this

§ References 18 and 19.

presentation is almost unique. However, the fact that both Noetzel and I have been fortunate in observing more than one case leads to the supposition that there may be other instances, which have remained unrecognized (2365 autopsies were performed in the eight-year interval between the discovery of the first and the second case at St. Elizabeths Hospital).

Among the well-known conditions of pigment deposition, Hallervorden-Spatz disease and allied conditions may be mentioned. Iron deposits in the pallidum and other basal ganglia nuclei have often been observed in routine neuropathologic investigations at St. Elizabeths Hospital. Strangely, as Zimmerman || has pointed out, patients with such deposits may have no clinical symptoms of lesions referable to these structures. Strassman [16] has discussed the relationship and occurrence of tissue iron and hemosiderin in the brain, particularly in such cases; he considered the increased iron content a manifestation of an involutional process irrespective of the age of the patient or duration or type of illness. There is, too, the so-called calcification of capillaries, which generally reacts positively for iron,, observed in cortical areas and dentate nuclei. The iron and calcium deposits described by Haymaker and associates [20] in a case of cytomegalic inclusion disease of the newborn is another example of a pathologic condition which bears some resemblance to our cases. In this case the walls of the lateral ventricles were most heavily involved; the right olfactory bulb and tract also contained many deposits. There were none in the cerebellum, basal ganglia, and brain stem. The olfactory tract involvement is of interest: The authors attributed the deposits in the bulb to the fact that in the embryo the subependymal matrix of the lateral ventricle is continuous with that of the olfactory bulb (Pearson; Humphrey; Yoss and Crosby ¶). This hypothesis would not serve to explain the pigmentation of the olfactory bulb and tract in the reported case, since there was no deposition in the walls of the lateral ventricles. Wegener, however, reported pigment in both these areas. His patient first showed symptoms of hemochromatosis at the age of 16, when an enlarged liver was found; pigmentation of the skin manifested itself not long afterward. This patient was a rare example of a familial case. One brother, and possibly the father, also suffered from hemochromatosis. Sheldon # believes that the disturbance of iron metabolism may exist for many years (present even at birth) before the patient gives overt evidence of the disease.

One may postulate whether the damage to the Purkinje cells might indicate a selective attack of the etiologic agent on these cells, known to be unusually sensitive to toxic effects. Where these cells disappear, as in hyperthermia, certain cerebellar atrophies, etc., there is, however, no deposition of iron or other pigment in this layer. The condition, then, presents puzzling and contradictory features. That the deposition of the pigments or some other agent stimulates reactive gliosis seems obvious. That the picture is not a purely cerebral manifestation is indicated by the presence of both pigments in liver cells, with hemofuscin predominating in both instances. This may be another example of the unexplained link between liver and cerebral pathology. The pigmentation of the liver is not believed to be the result of malnutrition, as postulated by Gillman and Gillman.[21] Control studies of livers from divers other conditions have failed to show significant pigmentation in this organ.

So far no uniformly acceptable theory has been advanced for the focal deposition of pigments in any of the conditions mentioned. Roizin,[22] in reporting an instance of a complex extrapyramidal syndrome accompanied by deposits of calcium and iron in the basal ganglia, dentate nuclei and granular layer of cerebellar folia, and other

|| Zimmerman, in discussion on Roizin,[22] p. 57.

¶ References cited by Haymaker and others.[20]

References 7 and 8.

areas, called such phenomena "neuropathologic selectivity combined with histochemical changes." He referred to the theory of Fahr, who believed a local factor might be combined with binding of calcium or iron ions by electrolytic colloidal systems. Merritt, in his discussion of these rare syndromes,* concluded that they were the result of "some inborn error of metabolism." Indeed, Sheldon, in his monumental study of hemochromatosis, could arrive at no more specific conclusion.† At present no better theory can be proposed.

The six recorded instances of this extraordinary type of pigmentation have been recognized only post mortem. To recognize these cases clinically, it is suggested that the occurrence of deafness without specific known cause, combined with progressive gait disturbance, again of unknown etiology, should lead the examining neurologist to suspect the presence of this condition. Chemical studies of blood and cerebrospinal fluid, with emphasis on the determination of abnormal amounts of iron, might then prove of significance.

In summary, the distribution of iron and hemofuscin pigments described appears to be a rare disturbance of metabolism, accompanied by slowly progressive loss of hearing and difficulty in walking. These symptoms appear to be a concomitant of the fact that the greatest damage is in the regions surrounding the lateral recesses of the fourth ventricle, and anterior lobe of the cerebellum. No theory as to the etiology of the disturbed metabolism can be advanced in the present state of our knowledge.

Summary

A case of hemochromatotic pigmentation of the central nervous system is described. The pigment was distributed in peripheral zones of the brain stem, olfactory bulbs and tracts, and certain cerebellar areas—anterior lobe, flocculus, and vermis. There were focal deposits in the cortex, pia-arachnoid, and thalamus. Focal gliosis and loss of myelin were demonstrated in areas of pigmentation.

The neurologic symptoms accompanying this pathologic picture are diminished auditory acuity and disturbances in gait.

Only five other cases showing similar pigment distribution and similar symptomatology have been recorded.

It is postulated that the iron and hemofuscin pigmentation result from a disturbance in metabolism.

* Merritt, H. H., in discussion on Roizin,[28] p. 57.

† References 7 and 8.

REFERENCES

1. Lewey, F. H., and Govons, S. R.: Hemochromatotic Pigmentation of the Central Nervous System, J. Neuropath. & Exper. Neurol. 1:29, 1942.

2. Neumann, M. A.: Hemochromatosis of the Central Nervous System, J. Neuropath. & Exper. Neurol. 7:19, 1948.

3. Noetzel, H.: Diffusion von Blutfarbstoff in der inneren Randzone und äusseren Oberfläche des Zentralnervensystems bei subarachnoidaler Blutung, Arch. Psychiat. 111:129, 1940.

4. Lillie, R. D.: Histopathologic Technique, Philadelphia, The Blakiston Company, 1948.

5. Noad, K. B., and Haymaker, W.: The Neurological Features of Tsutsugamushi Fever, with Special Reference to Deafness, Brain 76:113, 1953.

6. Courville, C. B.: Applied Anatomy of the 8th Nerve and Its Environs: The Cerebellopontine Angle, Laryngoscope 42:415, 1932.

7. Sheldon, J. H.: Hæmochromatosis, London, Oxford University Press, 1935.

8. Sheldon, J. H.: Iron Content of Tissues in Hæmochromatosis, with Special Reference to the Brain, Quart. J. Med. 21:123, 1927.

9. Wegener, H.: Über zwei Fälle von familiärer Hämochromatose, Ztschr. klin. Med. 107: 113, 1928.

10. McDougal, D. B., and Adams, R. D.: The Neuropathological Changes in Hemochromatosis, J. Neuropath. & Exper. Neurol. 9:117, 1950.

11. Cammermeyer, J.: Deposition of Iron in Paraventricular Areas of the Human Brain in Hemochromatosis, J. Neuropath. & Exper. Neurol. 6:111, 1947.

12. Noetzel, H.: Diffusion von Eisenpigment in das Gehirn, Excerpta med. VIII 8:864, 1955; Abstr. 3760.

13. Boyd, W.: A Text-Book of Pathology, Ed. 5, Philadelphia, Lea & Febiger, 1947.

14. Yater, W. M.; McNabe, P. E., and Horgan, E.: Clinicopathologic Types of Hemochromatosis, M. Ann. District of Columbia, pp. 28-35, 1932.

15. Hammes, E. M.: Reaction of the Meninges to Blood, Arch. Neurol. & Psychiat. 52:505, 1944.

16. Strassman, G.: Hemosiderin and Tissue Iron in the Brain, Its Relationship, Occurrence and Importance: A Study of 93 Human Brains, J. Neuropath. & Exper. Neurol. 4:393, 1945.

17. Pearse, A. G. E.: Histochemistry: Theoretical and Applied, Boston, Little, Brown & Company, 1953.

18. Skoog, T.: On the Vital Staining of the Central Nervous System: Experiments Devised to Break Down by Allergic Reaction the Blood-Brain Barrier in the Medullary Vestibular Region of Guinea Pigs, Acta oto-laryng. 25:365, 1937.

19. King, L. S.: Some Aspects of the Hematoencephalic Barrier, A. Res. Nerv. & Ment. Dis., Proc. (1937) 18:150, 1938.

20. Haymaker, W.; Girdany, B. R.; Stephens, J.; Lillie, R. D., and Fetterman, G. H.: Cerebral Involvement with Advanced Periventricular Calcification in Generalized Cytomegalic Inclusion Disease in the Newborn, J. Neuropath. & Exper. Neurol. 13:562, 1954.

21. Gillman, J., and Gillman, T.: Structure of the Liver in Pellagra, Arch. Path. 40:239, 1945.

22. Roizin, L.: Extrapyramidal Syndrome Akin to Hallervorden-Spatz and Fahr Disease: A Clinical Pathological report, Tr. Am. Neurol. A. 79: 56, 1955.

Ability to Discover Hidden Figures After Cerebral Lesions

HANS-LUKAS TEUBER, Ph.D.
and
SIDNEY WEINSTEIN, Ph.D., New York

Introduction

One of the universal aspects of perception is its selectivity. At any time, the sensory field is segregated into parts which acquire dominance for behavior and other parts which function as relatively indifferent background. Yet little is known of the physiologic basis for such selectivity. It is not limited to human perception, but appears in other mammals (Lashley,[30] Klüver,[24] Köhler[26]), in birds (Carrick,[6] Sumner,[41] Young[58]), in fish (Herter,* Schaller[39]), and perhaps even in higher invertebrates (Boycott,[5] von Frisch,[9] Ilse[19]).

Rubin[38] and the early Gestalt psychologists (Wertheimer,[54] Köhler,[27] Koffka[25]) have investigated one set of factors that determine what part of a sensory field will be selected as "figure" and what parts will tend to become "ground." These field factors, too, are surprisingly independent of structural differences in the perceiver's nervous system. Many figures that stand out easily for man do so for the rat, whether normally reared (Lashley[30]) or reared in darkness (Lashley and Russell,[31] Hebb[15]). Comparative studies thus far offer no direct clues to the neural basis of perceptual selectivity.

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* References 17, 18.

However, species differences do appear in the relative ease with which an organism can overcome concealing factors in the sensory field (Köhler,[26] Harlow and Settlage,[13] Klüver[24]), and, in this respect, there may be a crude correlation between complexity of the brain and perceptual ability. Similarly, brain lesions have been claimed to render the perceiver abnormally susceptible to factors which make for concealment.

The claims for such impairment after brain injury in man are based on various sources. In early studies (Poppelreuter[37]) the patient was confronted with "mixed" figures, in which overlapping contours were used to complicate perception (Werner and Strauss[53]). Soon after this came the use of reversible figures (Gelb and Goldstein,[10] Harrower[14]). The strongest evidence, however, was derived from "hidden figures," that is, complex line drawings in which known field factors had been employed to produce maximal concealment. Such figures had been constructed by Wertheimer,[54] Köhler,[27] and Gottschaldt,[12] but were first used with brain-injured subjects by Gelb and Goldstein[10] and are still being used in this fashion (Yacorzynski and Davis,[57] Teuber and associates,[45] Battersby and associates[2a]. Defective performance on such "hidden-figures" tests after brain injury has been demonstrated repeatedly, but there is little information on the nature of the impairment, its relation to other sequelae of cerebral injury, or its possible dependence on particular regions of the brain.

Available evidence points in two quite different directions: (1) The deficit may be a specific form of central visual disturbance associated with field defects and other signs of damage to central visual pathways

(Poppelreuter[37]), or (2) the deficit may appear with injury in any region of the brain, representing a basic disturbance which transcends the visual sense modality (Goldstein[11]). This second view agrees with the belief (Wertheimer,† Köhler,[27] Duncker,[7] Maier‡) that ability to unscramble perceptually complex figures is representative of reasoning.

Impairment as Sign of Visual Defect.—From the early work of Poppelreuter,[37] it would seem that impairment in perceiving hidden figures might be a specific sign of injury to central visual pathways. Such a view would be consistent with what is known about the course of recovery from lesions in these structures, and about the nature of persistent residual deficits.

Extensive subtotal lesions of the higher visual pathways in man usually result in an initial state of blindness, from which recovery occurs in minutes, days, or weeks (Poppelreuter,[37] Teuber and Bender[44]). Subtle deficits of visual perception apparently persist indefinitely in the remnants of the visual field, i.e., outside the area of residual scotoma. Such defects include impaired adaptation to light and darkness (Behr,[3] Krieger and Bender[28]), lowered fusion thresholds for flickering light (Teuber and Bender,§ Battersby[2]), reduced efficiency on tachistoscopic tests (Poppelreuter,[37] Teuber[42]), and marked difficulties with complex hidden figures (Teuber,[42] Teuber and associates[45]).

It would seem, therefore, that partial lesions of higher visual pathways in man have a twofold effect: a focal one, indicated by the circumscribed scotomata in the visual field, and a more general effect, viz., impaired ability to perceive hidden figures. But if visual field defect is a sufficient condition for the appearance of difficulties with hidden figures, it need not follow that field defects are necessary. This takes us to the second view.

Impairment as Sign of General Cerebral Dysfunction.—For Gelb and Goldstein,[10] difficulties with hidden figures are the prototype of nonspecific change in function, attributable to cerebral lesions in any lobe. Dedifferentiation of figure and ground appears in perception as impairment of contour formation, in the language sphere as impaired selection of words or phonemes. In fact, some of the aphasias are said to be effect rather than cause of impaired selectivity in reasoning. Partial support for these views comes from observation of defective performance on hidden-figure tasks in the absence of obvious visual field defects (Yacorzynski and Davis,[57] Werner and Strauss,[53] Teuber[42]). Particularly severe deficits are occasionally reported for aphasic patients (Bouman and Grünbaum,[4] Woerkom[56]). Some of this evidence, however, has been challenged.

Isserlin‖ and von Kuenburg,[29] who believe that language disorders in aphasia are specific and dissociable from impairment in perception and thought, have pointed out that administration of certain hidden-figure tasks involves a good deal of speech. Thus, the test used by Bouman and Grünbaum[4] (the Abelson Test[1]) requires detailed verbal instructions. The aphasics, therefore, may have done poorly because they did not understand what the task required.

An even more serious objection may be raised on the basis of data obtained by Weisenburg and McBride.[52] In a systematic study of test performance in aphasics, some deficits on nonlanguage tasks were found to coexist with verbal impairment, but the same nonlanguage deficits appeared in patients without aphasia. More recent reports have gone further still by suggesting that lesions of the right temporal lobe may lead to greater difficulties on certain performance tests than comparable lesions of the left temporal lobe (Hebb,[16] Milner,[34] Teuber and Weinstein[47]). If these results could be confirmed and extended to hidden-figure tasks, we would have evidence for a localizable impairment independent of both

† References 54, 55.
‡ References 32, 33.
§ References 43, 44.
‖ References 20-22.

aphasia and field defect. In that case, neither the view of a specifically visual basis for deficits on hidden figures nor the opposite view, of a (nonlocalizable) general disturbance, could be upheld.

What is needed is the administration of hidden-figure tests not only to groups of men with lesions in different lobes but to men with and without visual field defect, and with and without aphasia. We have considered these variables, as well as possible effects of irritative processes, by comparing brain-injured men with and without post-traumatic epilepsy. Other quantitatively defined signs, such as somatosensory impairment, were employed, in order to find possible lasting sensory defects which might result in inferior performance on a hidden-figure task. Finally, we have attempted to relate performance on a hidden-figure test to a traditional test of "intelligence" (AGCT).

Material and Methods

Subjects.—The 107 subjects for this study (64 brain-injured men and 43 controls) came from the same population of veterans on whom previous reports from this laboratory were based (Teuber,[42] Battersby,[3] Teuber and Mishkin,[46] Teuber and Weinstein,[47] Semmes and associates,¶ Weinstein,[50] Weinstein and associates[51]). All men in the present study had sustained their wounds in World War II, with the exception of one veteran of the recent Korean campaign. All were ambulatory at time of testing and came voluntarily to the laboratory to participate in various studies of sensory and motor functions. No attempt was made to select subjects.

Grouping by Locus of Lesion.—For purposes of analyzing test results, the subjects in the present study were grouped according to location of lesion and certain neurologic defects. Subdivision by location of lesion was accomplished as follows: After review of surgical and roentgenographic evidence, each subject's wound of entrance (and exit, if any), was charted on brain diagrams. Retained foreign bodies were recorded in the same fashion, as were known intracerebral missile tracts. This method records only the minimal extent of each lesion and does not yield sufficient evidence regarding depth of penetration or mass of tissue destroyed. Each lesion was classified as situated in

TABLE 1.—*Classification of Sixty-Four Brain-Injured Men*

*A. Distribution of Lesions by Lobe and Laterality**

Unilateral Lesions			Bilateral Lesions		
	Right	Left	N	Right	Left
F	7	4	7	F	F
			1	F	FT
			1	F	FPTO
P	1	1	1	P	PO
T	–	2	1	T	O
			1	TO	O
			1	TO	PTO
O	1	4	3	O	O
			1	O	FP
			1	O	PTO
FT	1	1	1	FT	F
FP	1	3	1	FP	F
FPT	–	3			
PT	1	–	1	PO	O
PO	3	–	1	PO	PO
TO	2	1	1	PTO	O
PTO	1	2	1	PTO	Cbllm
Cbllm	–	1	–		
Totals	18	22	24		

B. Summary Grouping by Locus of Lesion

Lobe	Unilateral Lesions			Bilateral Lesions			Totals
	Restricted to Indicated Lobe	Involving Additional Lobes in Same Hemisphere	Total Unilat. Lesion	Bilat. for Indicated Lobe	Unilat. for Indicated Lobe and Involving Additional Lobes in Opposite Hemisphere	Total Bilat. Lesion	Unilat. and Bilat. for Each Lobe
Frontal	11	9	20	11	1	12	32
Parietal	2	14	16	2	8	10	26
Temporal	2	12	14	1	8	9	23
Occipital	5	9	14	9	5	14	28

* F,P,T,O, and Cbllm stand for frontal, parietal, temporal, occipital, and cerebellum, respectively.

¶ Semmes and associates.[50] Semmes, J.; Weinstein, S.; Ghent, L., and Teuber, H. L.: Changes in Somatic Sensation After Penetrating Brain Wounds in Man, paper in preparation.

the frontal, parietal, temporal, or occipital lobe, or combinations of these, and in the right or left hemisphere or both. The resulting classification of the 64 brain-injured subjects is given in Table 1.

Comparisons were made among mutually exclusive groups, in the following manner: A subject with, say, a frontoparietal lesion on the left was included in the "frontal" group, the "parietal" group, and the "left" group, as well as the "nontemporal" and "nonoccipital" groups. Each group was compared with the remainder of the brain-injured sample; i.e., the men in the frontal group were compared with all subjects who did not have involvement of the frontal lobes (nonfrontal groups), and correspondingly for all other subgroups.

The scores of the resulting groups were compared by means of separate analyses of variance, namely, controls *vs.* frontal lesions *vs.* nonfrontal lesions, and similarly for the other lobes. A fifth analysis concerned controls *vs.* right unilateral *vs.* left unilateral *vs.* bilateral lesions.

Subjects were also grouped according to presence or absence of visual field defects, somatosensory deficits, aphasia, or post-traumatic epilepsy. Visual field defect was defined as before (Teuber and Bender [4]), as inability, in homonymous retinal regions, to discriminate presence from absence of a stationary circular white target subtending 1 degree. These fields were taken separately for each eye, on a Ferree-Rand perimeter at 330 mm. distance from the cornea, under 7 f-c. illumination.

Presence or absence of aphasia was determined by the consensus of the laboratory staff (including us). In all cases in which aphasia was judged to be present, the subjects themselves complained of difficulties with language, dating from their injury. No attempt was made in the present study to classify the individual language disorders.

For the purpose of this study, post-traumatic epilepsy was defined as occurrence of one or more unequivocal seizures or seizure equivalents (Jacksonian sensory attacks, psychomotor episodes) after inclusion of the case into the research program at the laboratory (a minimum of about seven years for veterans of World War II).

Somatosensory defects were defined in terms of the subject's performance on four separate tests, i.e., tests of passive movement, light touch, two-point discrimination, and point localization. These tests will be described in detail in a forthcoming publication (Semmes and associates #). Passive movement was rated as normal or defective; for all other somatosensory measures, impairment was judged to be present if a subject's threshold ex-

Semmes, J.; Weinstein, S.; Ghent, L., and Teuber, H. L.: Changes in Somatic Sensation After Penetrating Brain Wounds in Man, paper in preparation.

TABLE 2.—*Distribution of Defects of Sixty-Four Brain-Injured Subjects**

N	Aphasia	Epilepsy	Field Defect	S1	S2	S3	S4	N	Aphasia	Epilepsy	Field Defect	S1	S2	S3	S4
1	X	X	X	0	0	0.001	0.01	1	0	X	X	X	0.001	..	..
1	X	X	X	0	0	0.001	0	1	0	X	X	0	0	0	0
1	X	X	X	0	0.01	0	0	1	0	X	X	..	..	..	..
1	X	X	X	..	..	..	..	1	0	X	0	X	0	0	0
1	X	X	0	X	0.001	0.001	0.001	1	0	X	0	0	0	0.001	0
1	X	X	0	X	0	0	0	1	0	X	0	0	0	0	0.01
1	X	X	0	..	..	..	..	2	0	X	0	..	..	..	..
1	X	0	X	X	0.001	0.001	0.001	5	0	0	X	0	0	0	0
1	X	0	X	0	0	0.001	0	1	0	0	X	..	..	..	..
1	X	0	X	0	0.01	..	..	3	0	0	X	..	..	..	..
2	X	0	X	0	0	0	0	1	0	0	0	X	0	0.001	0
2	X	0	X	..	..	..	..	1	0	0	0	X	0	..	0.01
1	X	0	0	X	0.001	0.001	0.001	1	0	0	0	0	0.001	0	0.01
1	X	0	0	0	0.001	0.001	0.001	1	0	0	0	0	0	0.001	0
1	X	0	0	X	0	..	..	1	0	0	0	0	0	0	0.001
1	X	0	0	0	0	..	..	2	0	0	0	0	0	0	0.01
1	X	0	0	..	..	..	..	5	0	0	0	0	0	0	0
1	0	X	X	0	0.01	0.001	0	15	0	0	0	..	..	..	..

* Each column shows presence or absence of defect for N men, indicated in each row. S1 refers to defective appreciation of passive movements; S2, to defective touch sensitivity; S3, defective two-point discrimination; S4, defective point localization. X indicates presence of defect; 0, absence of defect; 0.01, presence of defect at 0.01 level; 0.001, presence of defect at 0.001 level. Diaereses (..) indicate absence of data.

ceeded the mean of a larger control group at the 0.01 or 0.001 level.

The influence of these defects upon performance in the hidden-figure task was evaluated by means of a series of analyses of variance, viz., controls *vs.* subjects with defects in passive movement *vs.* subjects with sensory defects exclusive of passive movement *vs.* subjects without sensory defects. Corresponding analyses of variance were performed for the other measures of sensory defect. The role of severity of sensory defect was also explored by comparing controls *vs.* subjects with sensory defects (any or all) not exceeding the 0.01 level *vs.* subjects with sensory defects (any or all) reaching the 0.001 level *vs.* subjects without sensory defects.

Analyses for aphasia, epilepsy, and visual field defect were performed for controls and the brain-injured groups with and without the specified defect. The grouping of the 64 subjects according to presence or absence of defect is given in Table 2.

Procedure.—The hidden figures employed in the present study were those devised by Gottschaldt,[19] and used previously. They are illustrated in full in Thurstone's Factorial Study of Perception.[48] A sample page is given in Figure 1. The five sections of the test were given in fixed order from I to V, with the following time limits, respectively: two, one, three, four, and four minutes. Great care was taken in explaining the task to the subject by means of the demonstration items. The few cases of brain injury with severe motor impairment of the preferred hand (N=3) were permitted to use their other hand in tracing the forms. Since there was a greater proportion of controls with motor impairment of the preferred hand due to nerve injury (N=5), this factor was considered controlled. Scoring was based on total number of items correctly traced within the time limits.

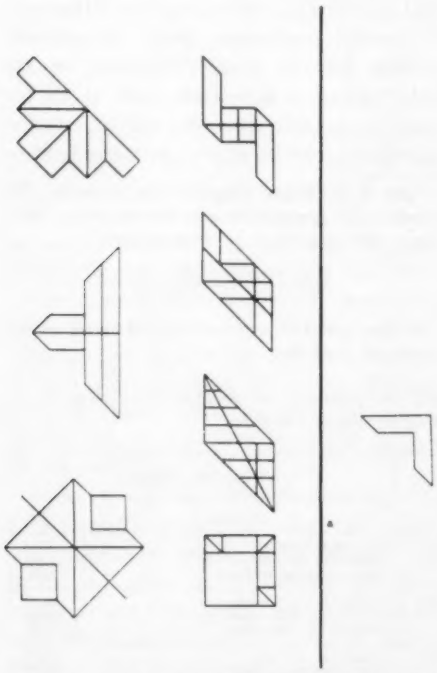

Fig. 1.—Sample page of Gottschaldt Test. The subject is required to find the figure at the top within each of the lower (embedding) figures, and to trace it completely with pencil within each of the embedding figures.

Results

Analysis of results according to locus of lesion (Table 3) revealed that the control group surpassed each of the brain-injured subgroups to a significant extent ($P<0.001$); however, none of the brain-injured subgroups differed one from the other in any analysis (Fig. 2).

A similar result appeared when the brain-injured subjects were classified on the basis of the various somatosensory defects. Means for each of these subgroups (with the exception of those with defective point localization) fell significantly below the control-group mean (P values ranged from <0.05 to <0.01). The same was true for men with any sensory defect reaching the 0.001 level ($P<0.01$), but not for those with only the less severe (0.01) defects. No other group comparisons yielded significant differences.

Comparisons of scores for the symptom groupings, viz., visual field defect, epilepsy, and aphasia, are summarized in Table 4. In each analysis, the controls surpassed each of the brain-injured subgroups ($P<0.01$ or <0.001). However, dissociation among brain-injured subgroups appeared only in the analysis for aphasia. The performance

TABLE 3.—*Mean Scores (Items Correctly Traced), and Summary of Analyses of Variance,* for Groups Divided by Locus of Lesion*

M	*N*	Groups	*MS*	*F*
33.63	43	Control *vs.*	1605.12	10.78†
25.75	32	Frontal *vs.*	148.94	
20.66	32	Nonfrontal		
33.63	43	Control *vs.*	1401.28	9.17†
23.62	26	Parietal *vs.*	152.86	
22.92	38	Nonparietal		
33.63	43	Control *vs.*	1405.89	9.20†
22.52	23	Temporal *vs.*	152.77	
23.58	41	Nontemporal		
33.63	43	Control *vs.*	1429.43	9.38†
22.07	28	Occipital *vs.*	152.31	
24.08	36	Nonoccipital		
33.63	43	Control *vs.*	943.76	6.12†
22.50	18	R Unilateral *vs.*	154.06	
22.73	22	L Unilateral *vs.*		
24.17	24	Bilateral		

* The results of five analyses of variance are given. The first value of "mean squares" (*MS*) in each analysis is that between groups; the second is within groups. The *df* values are 2 and 104, respectively, with the exception of the final analysis, in which they are 3 and 103.
† $P<0.001$.

of brain-injured subjects with aphasia was not only far below that of the controls ($P<0.001$), but also below that of the brain-injured subjects without aphasia ($P<0.01$). The latter, in turn, performed more poorly ($P<0.01$) than the controls (Fig. 3).

This result was analyzed further in order to see whether the low scores of the aphasics might not reflect merely some nonspecific intellectual impairment. Scores on the Army General Classification Test (AGCT, First Civilian Edition) obtained

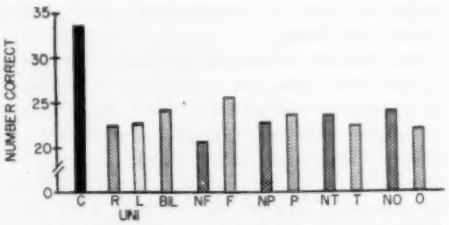

Fig. 2.—Mean number of figures correctly traced by controls (*C*) and brain-injured subjects grouped according to location of lesion. *R*, right unilateral lesion; *L*, left unilateral lesion; *BIL*, bilateral lesion; *F*, *P*, *T*, and *O*, indicate frontal, parietal, temporal, and occipital, respectively; *NF*, *NP*, *NT*, and *NO* indicate nonfrontal, nonparietal, etc.

within the same year, for the most part, as the Gottschaldt scores, were available for 25 controls, 13 men with brain injury and aphasia, and 21 men with brain injury without aphasia. An analysis of covariance was performed, with AGCT scores as predictor variable, for controls *vs.* aphasics *vs.* nonaphasics. The analysis yielded an F of 8.61 ($P<0.001$), indicating that differences in general intelligence could not entirely account for the group differences on the hidden-figure task.* This result is all the more remarkable since the product-moment correlation coefficient (r) between hidden-

* Dr. L. S. Kogan suggested the following procedure as an approximation to the covariance technique when regression is heterogeneous.

$$F=\frac{S_T-S_2}{S_2}\cdot\frac{N-2k}{2k-2}$$

Walker and Lev may be referred to for explanation of symbols.

TABLE 4.—*Mean Scores (Items Correctly Traced), and Summary of Analyses of Variance* for Groups Classified According to Major Symptom*

M	*N*	Groups	*MS*	*F*	*t*'s Between Groups	
					Groups	*t*'s
33.63	43	Controls	1633.50	11.01†	Control *vs.* epilepsy	4.24†
18.50	16	Epilepsy			Control *vs.* no epilepsy	3.46†
24.77	48	No epilepsy	148.39		Epilepsy *vs.* no epilepsy	1.79
33.63	43	Controls	1494.30	9.89†	Control *vs.* field defect	4.05†
20.96	24	Field defect			Con. *vs.* no field defect	3.36‡
24.55	40	No field defect	151.07		Field *vs.* no field defect	1.13
33.63	43	Control	1908.66	13.34†	Control *vs.* aphasia	5.02†
17.05	19	Aphasia			Control *vs.* no aphasia	3.07‡
25.80	45	No aphasia	143.10		Aphasia *vs.* no aphasia	2.68‡

* The results of three analyses of variance are given. The first entry for "mean squares" (*MS*) in each analysis is that between groups; the second is that within groups. The *df* values are 2 and 104 respectively.
† $P<0.001$.
‡ $0.001<P<.01$.

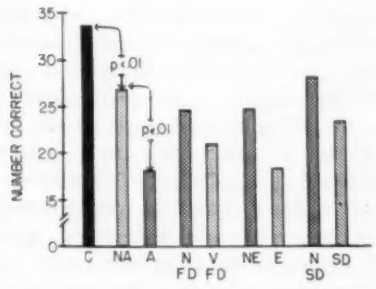

Fig. 3.—Mean number of figures traced correctly by controls (*C*), and by brain-injured subjects grouped according to presence or absence of aphasia (*A*), visual field defect (*VFD*), epilepsy (*E*), and somatosensory defect (*SD*). Absence of a given defect is indicated by *N*.

figure scores and AGCT scores was positive and significant for the control group ($r=0.83$; $P<0.001$) and for the nonaphasic brain-injured group ($r=0.69$; $P<0.001$). By contrast, the r between hidden-figure scores and AGCT scores in the aphasic group was negative and not significant (-0.31), and differed significantly from the r's of the other groups.

Comment

Our results show that impairment on hidden-figure tasks follows lesions in any lobe of the brain. It also appears irrespective of presence or absence of visual or sensory symptoms. In all these regards, deficits on the hidden-figure test turned out to be a nonspecific sequel of penetrating brain lesions. However, impairment was significantly related to the presence of aphasia, since aphasics, as a group, did considerably worse than nonaphasic brain-injured subjects, who were surpassed, in turn, by the controls.

Role of Field Defect.—Among the least expected findings of this study is the one concerning visual field defects. Injuries of higher visual pathways resulting in permanent field defects were not a necessary condition for difficulties with hidden figures. The impairment exists with and without concomitant symptoms in the same sense modality through which the task is perceived. In fact, we need not assume that the impairment is limited to vision. A tactile analogue of the task might have brought out similar deficits. Lacking such experimental variations of the task, one might wonder whether the symptom was unitary—i.e., did men with field defects fail on our task in a different way, and for a different reason, than those without field defect? Observations on test performance give no support to this view, since there were no indications that men with and without field defects failed on different items, or worked at different speeds. Both groups showed the same kind of impairment, qualitatively as well as quantitatively.

Such a conclusion differs from that of Poppelreuter,[37] who considered impairment in perception of complex figures as a symptom tied specifically to other forms of visual dysfunction. However, Poppelreuter's different impression may be due to the fact that he studied the early after-effects of occipital lesions, with correspondingly greater visual disturbances than in our groups (tested 10 years after the wounding). Moreover, Poppelreuter relied primarily on "mixed" figures, rather than on hidden figures of the type here used.

Role of Aphasia.—In contrast to our nondifferential results for visual field defects was the definite association between aphasia and severe impairment on the hidden-figure task. This observation might appear incompatible with the lack of association between test impairment and specific locus of lesion. However, one must remember that the nonaphasic group also showed significant deficits when compared with the controls. It was the severity of the impairment that distinguished aphasics from nonaphasics on this task. The result is compatible with the notion that maximal impairment was caused by those lesions which were either critically placed in several lobes or so extensive that a permanent aphasia was produced.

It is unlikely that the greater impairment of the aphasics was attributable to their language defects as such. There were no indications that the aphasics had failed to

understand the instructions. They failed most frequently by "losing track" of the direction of crucial lines in the network of interfering contours. In this respect, their difficulties were of the same kind as those encountered by nonaphasic subjects and controls.

Nor can one equate the impairment of the aphasics on the hidden-figure task with general intellectual deficit. It is true that in controls and in the nonaphasic brain-injured groups there were significant positive correlations between scores on AGCT and the hidden-figure task. In the aphasic group, however, the correlations between AGCT scores and hidden-figure scores were uniformly negative, although nonsignificant. Furthermore, inferiority of the aphasics on hidden-figure tasks remained a significant result when differences in AGCT scores were controlled by analysis of covariance. The deficit revealed by the hidden-figure test is thus not identical with impairment on the AGCT. The conclusion seems justified that aphasia is associated with a deficit which transcends language, but which is not identical with intellectual deterioration.

Impairment on hidden figures does not stand alone in this respect. We have recently demonstrated that aphasics achieved significantly lower scores than nonaphasic brain-injured subjects on another nonverbal task: a conditional reaction (Weinstein and associates [51]). In this task, subjects had to choose a triangle rather than a circle when both figures appeared on a horizontally striped background, and the circle rather than the triangle when the background stripes were vertical. Here, again, aphasics did significantly worse than nonaphasic brain-injured subjects, who, in turn, did worse than controls. The inferiority of the aphasics again remained statistically significant when differences on the AGCT were controlled by analysis of covariance.

Both types of nonverbal deficit found for the aphasics—impairment on hidden figures and on conditional reaction—were also present in subjects who did not show aphasia and had lesions of the right (and presumably nondominant) hemisphere. However, the group with right-hemisphere involvement showed the deficits to a significantly less degree. In this respect, our findings do not agree with expectations based on results of Weisenburg and McBride,[52] who found equal amounts of impairment on nonverbal tasks in aphasics with left-hemisphere lesions and in nonaphasic patients with lesions of the right hemisphere. Our findings likewise restrict the generality of conclusions one might draw from observations by Hebb,[16] Milner,[34] and us (Teuber and Weinstein [47]), who noted maximal deficits on certain nonverbal tasks in subjects with right temporal lesions.

The severe impairment of aphasics on hidden figures and conditional reaction which we have found does not encourage interpretations of the aphasias as specific losses of associations or engrams for linguistic patterns (Isserlin,† Kleist,[23] Nielsen [35]). Instead, our observations support the view that an important aspect of aphasia is defective organization or selection of material (linguistic as well as nonlinguistic), a disturbance manifested only partly in the obvious difficulties with linguistic reception or expression (Pick,[36] Goldstein,[11] Woerkom [56]). We do not wish to imply that all types of aphasia are alike in this respect; appropriate subdivision of a larger group of aphasics might reveal differences. Yet the defect in organization must be a sufficiently prominent feature of several forms of aphasia; otherwise, it would not have shown itself so clearly in our group, which combined aphasics irrespective of type.

Problem of Localization.—Our analysis of impairment on hidden figures has shown no relation to any concomitant defect with the exception of aphasia; similarly, there was a striking absence of localization for this deficit. Subjects performed poorly with injury in any lobe. One might say that such ubiquity of deficit merely reflects diffuseness of cerebral lesions in this study.

† References 20-22.

According to this view, it is the lesion rather than the symptom that is generalized. This view, however, becomes difficult to maintain, since certain differential test results have previously been obtained in our laboratory for the same population (Teuber and Mishkin,[46] Semmes and associates,[40] Weinstein[50]). Failure to find a localization for deficits on hidden figures must be referred to the nature of the task rather than the groups tested.

The generality of the deficit may turn out to be trivial if the task was so complex that a localized impairment could not be expected. If adequate performance on a test depends on a number of different functions each of which is crucial, then any lesion sufficient to upset one of them may lead to significant general impairment. In its most general form, the argument is unanswerable. However, it is not clear how subordinate elements of the Gottschaldt task could be identified.

A great deal of work on localization of cerebral function has been guided by the implicit argument that nonspecific effects of lesions are to be classed as preliminary results, awaiting analysis into separate aspects susceptible of separate localization. The argument amounts to a *petitio principii;* its acceptance would forever prevent discovery of general effects of cerebral lesions, which might coexist with specific effects already observed. For the time being, we prefer to proceed in empirical fashion and to place equal confidence in the nonspecific effects of brain injury, as revealed by the hidden-figure task, and the specific (localizable) effects revealed by so many other tasks thus far employed.

We may therefore conclude that cerebral lesions in man have twofold effects: specific and general; which one appears is a function of the tests employed. At this stage, one should not stress one type of finding at the expense of the other, since no one has pushed the analysis of behavior far enough to permit assignment of empirical weights to specific or general symptoms. The situation is similar in current animal studies; there some tests bring out defects which are clearly localizable (delayed response, certain visual discrimination tasks), while performance on other tests, e.g., certain conditional reactions, is affected by injury in any lobe. Such findings recall the belief of Flourens,[8] who assigned to all major sectors of the forebrain an *action commune,* in addition to their *action propre.* If one considers the wide scope of perceptual selectivity in higher forms, one can understand its dependence on such common action of the brain, and its nonspecific decline, after brain injury in man.

Summary

Sixty-four men with traumatic, penetrating brain wounds, and forty-three controls with peripheral-nerve injury were tested on a hidden-figure task. Although none of the brain-injured groups, differentiated on the basis of locus of lesion, differed one from the other, all brain-injured subgroups were significantly inferior to controls. When the brain-injured population was subdivided according to presence or absence of neurologic defect, neither those with visual field defect, nor those with epilepsy, nor those with somatosensory defect were more impaired than brain-injured persons without such defects. The group with aphasia, however, performed significantly worse than the nonaphasic brain-injured group, which, in turn, was surpassed by the controls. These differences remained, even after statistical elimination of present differences in intelligence.

REFERENCES

1. Abelson, A. R.: The Measurement of Mental Ability in Backward Children, Brit. J. Psychol. 4:268-314, 1911.

2. Battersby, W. S.: The Regional Gradient of Critical Flicker Frequency After Frontal or Occipital Injury, J. Exper. Psychol. 42:59-68, 1951.

2a. Battersby, W. S.; Krieger, H. P.; Pollack, M., and Bender, M. B.: Figure-Ground Discrimination and the "Abstract Attitude" in Patients with Cerebral Neoplasms, A. M. A. Arch. Neurol. & Psychiat. 70:703-712, 1953.

3. Behr, C.: Die Erkrankungen der Sehbahn

vom Chiasma aufwärts, in Kurzes Handbuch der Ophthalmologie, F. Schieck and A. Brückner, Editors, Berlin, Springer-Verlag, 1931, Vol. 6, Auge und Nervensystem, pp. 245-323.

4. Bouman, L., and Grünbaum, A. A.: Experimentell-psychologische Untersuchungen zur Aphasie und Paraphasie, Ztschr. ges. Neurol. u. Psychiat. 96:481-538, 1925.

5. Boycott, B. B.: Learning in Octopus Vulgaris and Other Cephalopods, Pubbl. Staz. zool. Napoli 25:67-93, 1954.

6. Carrick, R.: Experiments to Test the Efficiency of Protective Adaptations in Insects, Tr. Roy. Entomol. Soc. London 85:131-139, 1936.

7. Duncker, K.: On Problem-Solving, translated by L. S. Lees, Psychological Monograph 58; No. 5, American Psychological Association, 1945.

8. Flourens, M. J. P.: Recherches expérimentales sur les propriétés et les fonctions du système nerveux, dans les animaux vertébrés, Paris, Crevot, 1824.

9. von Frisch, K.: Der Farbensinn und Formensinn der Biene, Zool. Jahrb., Abt. allg. Zool. u. Physiol. 35:1-182, 1914.

10. Gelb, A., and Goldstein, K.: Psychologische Analysen hirnpathologischer Fälle, Leipzig, Johann Ambrosius Barth, 1920.

11. Goldstein, K.: Die Lokalisation in der Grosshirnrinde, in Handbuch der normalen und pathologischen Physiologie, A. Bethe and E. Fischer, Editors, Berlin, Springer-Verlag, 1927, Vol. 10, pp. 600-842.

12. Gottschaldt, K.: Über den Einfluss der Erfahrung auf die Wahrnehmung von Figuren, Psychol. Forsch. 8:261-317, 1926; 12:1-87, 1929.

13. Harlow, H. F., and Settlage, P. H.: Comparative Behavior of Primates: VII. Capacity of Monkeys to Solve Patterned String Tests, J. Comp. Psychol. 18:423-435, 1934.

14. Harrower, M. R.: Changes in Figure-Background Perception in Patients with Cortical Lesions, Brit. J. Psychol. 30:47-51, 1939.

15. Hebb, D. O.: Innate Organization of Visual Activity: I. Perception of Figures by Rats Reared in Total Darkness, J. Genet. Psychol. 51:101-126, 1937.

16. Hebb, D. O.: Intelligence in Man After Large Removals of Cerebral Tissue: Deficits Following Right Temporal Lobectomy, J. Gen. Psychol. 21:437-446, 1939.

17. Herter, K.: Dressurversuche an Fischen, Ztschr. vergl. Physiol. 10:688-711, 1929.

18. Herter, K.: Weitere Dressurversuche an Fischen, Ztschr. vergl. Physiol. 11:730-748, 1930.

19. Ilse, D.: Zur "Formwahrnehmung" der Tagfalter: I. Spontane Bevorzugung von Formmerkmalen durch Vanessen, Ztschr. vergl. Physiol. 17: 537-556, 1932.

20. Isserlin, M.: Die pathologische Physiologie der Sprache, Ergebn. Physiol. 29:129-244, 1929.

21. Isserlin, M.: Die pathologische Physiologie der Sprache, Ergebn. Physiol. 33:1-102, 1931.

22. Isserlin, M.: Die pathologische Physiologie der Sprache, Ergebn. Physiol. 34:1065-1144, 1932.

23. Kleist, K.: Gehirn-Pathologie vornehmlich auf Grund der Kriegserfahrungen, in Handbuch der ärztlichen Erfahrungen im Weltkriege, Leipzig, Johann Ambrosius Barth, 1934, Vol. IV, Pt. 2, pp. 343-1408.

24. Klüver, H.: Behavior Mechanisms in Monkeys, Chicago, University of Chicago Press, 1933.

25. Koffka, K.; Principles of Gestalt Psychology, New York, Harcourt, Brace and Company, Inc., 1935.

26. Köhler, W.: The Mentality of Apes, translated by Ella Winter, London, Routledge & Kegan Paul, 1925.

27. Köhler, W.: Gestalt Psychology, New York, Liveright Publishing Corporation, 1947.

28. Krieger, H. P., and Bender, M. B.: Dark Adaptation in Perimetrically Blind Fields, A. M. A. Arch. Ophth. 46:625-636, 1951.

29. von Kuenburg, M.: Über das Erfassen einfacher Beziehungen von anschaulichem Material bei Hirngeschädigten, insbesondere bei Aphasischen, Ztschr. ges. Neurol. u. Psychiat. 85:120-163, 1923.

30. Lashley, K. S.: The Mechanism of Vision: XV. Preliminary Studies of the Rat's Capacity for Detail Vision, J. Gen. Psychol. 18:123-193, 1938.

31. Lashley, K. S., and Russell, J. T.: The Mechanism of Vision: XI. A Preliminary Test of Innate Organization, J. Genet. Psychol. 45:136-144, 1934.

32. Maier, N. R. F.: Reasoning in Humans: I. On Direction, J. Comp. Psychol. 10:115-143, 1930.

33. Maier, N. R. F.: Reasoning in Humans: II. The Solution of a Problem and Its Appearance in Consciousness, J. Comp. Psychol. 12:181-194, 1931.

34. Milner, B.: Intellectual Function of the Temporal Lobes, Psychol. Bull. 51:42-62, 1954.

35. Nielsen, J. M.: Agnosia, Apraxia, Aphasia, New York, Paul B. Hoeber, Inc., 1946.

36. Pick, A.: Die agrammatischen Sprachstörungen, Berlin, Springer-Verlag, 1913.

37. Poppelreuter, W.: Die psychischen Schädigungen durch Kopfschuss im Kriege 1914-16, Leipzig, L. Voss, 1917, Bd. I.

38. Rubin, E.: Synsoplevede Figurer, Copenhagen, Gyldendal, 1915; German translation, Visuell wahrgenommene Figuren, Copenhagen, Gyldendal, 1921.

39. Schaller, A.: Sinnesphysiologische und psychologische Untersuchungen an Wasserkäfern und Fischen, Ztschr. vergl. Physiol. 4:370-464, 1926.

40. Semmes, J.; Weinstein, S.; Ghent, L., and

Teuber, H. L.: Spatial Orientation in Man After Cerebral Injury: I. Analyses by Locus of Lesion, J. Psychol. 39:227-244, 1955.

41. Sumner, F. B.: Does "Protective Coloration" Protect? Results of Some Experiments with Fishes and Birds, Proc. Nat. Acad. Sc. 10:559-564, 1934.

42. Teuber, H. L.: Neuropsychology, in Recent Advances in Diagnostic Psychological Testing, Springfield, Ill., Charles C Thomas, Publisher, 1950, Chap. 3.

43. Teuber, H. L., and Bender, M. B.: Critical Flicker Frequency in Defective Fields of Vision, Fed. Proc. 7:123-124, 1948.

44. Teuber, H. L., and Bender, M. B.: Alterations in Pattern Vision Following Cerebral Lesions, J. Gen. Psychol. 40:37-57, 1949.

45. Teuber, H. L.; Battersby, W. S., and Bender, M. B.: Performance of Complex Visual Tasks After Cerebral Lesions, J. Nerv. & Ment. Dis. 114: 413-429, 1951.

46. Teuber, H. L., and Mishkin, M.: Judgment of Visual and Postural Vertical After Brain Injury, J. Psychol. 38:161-175, 1954.

47. Teuber, H. L., and Weinstein, S.: Performance on a Formboard-Task After Penetrating Brain Injury, J. Psychol. 38:177-190, 1954.

48. Thurstone, L. L.: A Factorial Study of Perception, Chicago, University of Chicago Press, 1944.

49. Walker, H. M., and Lev, J.: Statistical Inference, New York, Henry Holt & Company, Inc., 1953.

50. Weinstein, S.: Time Error in Weight Judgment After Brain Injury, J. Comp. & Physiol. Psychol. 48:203-207, 1955.

51. Weinstein, S.; Teuber, H. L.; Ghent, L., and Semmes, J.: Complex Visual Task Performance After Penetrating Brain Injury in Man, Am. Psychologist 10:408, 1955.

52. Weisenburg, T. H., and McBride, K. E.: Aphasia: A Clinical and Psychological Study, New York, Commonwealth Fund, Division of Publications, 1935.

53. Werner, H., and Strauss, A. A.: Pathology of Figure-Background Relation in the Child, J. Abnorm. & Social Psychol. 36:236-248, 1941.

54. Wertheimer, M.: Untersuchungen zur Lehre von der Gestalt, Psychol. Forsch. 4:301-350, 1923.

55. Wertheimer, M.: Productive Thinking, New York, Harper & Brothers, 1945.

56. Woerkom, W. v.: Über Störungen im Denken bei Aphasiepatienten: Ihre Schwierigkeiten beim Erfassen elementarer Beziehungen, Monatsschr. Psychiat. u. Neurol. 59:250-322, 1925.

57. Yacorzynski, G. K., and Davis, L.: An Experimental Study of the Frontal Lobes in Man, Psychosom. Med. 7:97-107, 1945.

58. Young, R. T.: Some Experiments on Protective Coloration, J. Exper. Zool. 20:457-507, 1916.

Case Reports

Alteration of Consciousness: Tumor of the Reticular Activating System

N. L. MASON-BROWNE, M.B., Essondale, B. C., Canada

CONSCIOUSNESS is a word with many meanings. Schiller [1] remarked that it may connote attending, sensing, being alive, being responsive to stimuli, having insight, being able to communicate, and the psychoanalysts give it another interpretation. It can also be described as a state of passive awareness independent of speech or movement. Such a definition applies to crude as distinct from discriminative consciousness and will be the definition used here.

Le Gros Clarke [2] has drawn attention to the function of the thalamic and brain-stem reticular system as the possible structural basis of what may be called a general background of consciousness. Interest in the reticular system as the activator of consciousness originates largely from animal experimental work of Magoun [3] and others. Clinical evidence in support of this hypothesis is rare, and it is partly for this reason that a case admitted to the Royal Edinburgh Hospital for Mental and Nervous Disorders is of special interest. The case was one of brain stem tumor, and the predominant symptom was alteration of consciousness as defined above. It is felt to be important that data obtained in animal experiment should be supported in this way by clinical findings in man.

Throughout the fiber laminae of the thalamus, hypothalamus, midbrain, pons, and medulla are diffusely scattered formations of small cells, the so-called "intralaminar nuclei." These nuclei, together with the midline nuclei of the thalamus, form the brain-stem reticular system, which has diffuse nonspecific cortical and rhinencephalic projections. Embedded among the thalamic intralaminar nuclei are to be found the principal nuclei of the thalamus, which have, in contrast, well-known specific projections of the cortex. The principal nuclei are held to be responsible only for specific modes of discriminative awareness appearing on the back cloth of a general nonspecific consciousness.

The intralaminar nuclei of the reticular system appear to control rhythmical activity of the cerebral cortex. Animal experiment has also demonstrated that stimulation of these nuclei produces apparent alterations in conscious awareness similar to petit mal seizures in man. It has been postulated, therefore, that cortical activity and consciousness are dependent upon controlling function of the reticular system, that this system maintains a state of consciousness, and that reduction in activity of the system produces reduction of consciousness.

Work by Moruzzi and Magoun [4]; Starzl, Taylor, and Magoun*; Magoun [7] alone, and others has demonstrated the existence of this system, which has been shown to receive visual, auditory, somatic, and visceral impulses. It is probable, however, that the reticular system is more than a relay station on conduction routes to the cortex, with its well-known centrifugal and centripetal projection paths. Evidence for this assumption lies in the fact that incoming fibers to the reticular system are not in any way organized. The whole system diffusely subserves all sensory modalities. The system would therefore seem to be one consisting of neurons all interrelated by numerous relays, and all capable of equivalent discharge by all types of stimulation, whether these are

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Crease Clinic of Psychological Medicine.

* References 5, 6.

peripherally or directly produced. It follows from this that the system cannot be concerned so much with the conscious differentiation of one sensation from another as with a state of consciousness, of basic awareness, common to all modalities of sensation. Thus, the reticular system may be thought of, in the light of present knowledge, as an activating system necessary for consciousness. It would seem that both this activating system, with its at present unknown cortical connections, and the principal nuclei of the thalamus, with their known projection systems, are simultaneously activated by peripheral stimuli—the one subserving a general substratum of consciousness or awareness, and the other, specific modalities.

Experimental work has also been done to demonstrate the effects of interference with this activating or reticular system.

In 1939 Ranson [8] showed experimentally that lesions in the lateral border of the hypothalamus and caudally as far as the mammillary bodies produced somnolence, while catalepsy followed damage to the brain stem from the ventral hypothalamus to the third nerve. Ranson considered that the posterior hypothalamus was implicated in consciousness. It now seems probable that the somnolence was due, rather, to lesions in the hypothalamic components of the reticular system.

Artificial destructive lesions in the reticular system have produced profound loss of consciousness. The effects of lesions made by electrodes anywhere on the reticular system have also been investigated by Lindsley † and French and Magoun.[11] It was shown that such lesions produce what was called "chronic somnolence," with extreme unresponsiveness, immobility, failure of purposive movement, and varying degrees of hypokinesia to complete akinesia, and that these effects do not vary with the site within the reticular system of the artificial lesion. Experiment further showed that the long motor and sensory systems of these hypokinetic experimental subjects had not been affected. It was also demonstrated that the extent of somnolence and hypokinesia produced was dependent upon the quantitative amount of reticular system involved in the artificially produced lesion. Since it has been shown that the system diffusely subserves all sensory modalities, all this evidence would seem to support further the hypothesis that the reticular system acts as a whole, influences the whole cortex diffusely, and responds as a unit to all modalities of sensation. It is interesting to note that in some of the subjects of the experiments in which lesions of the brain stem were electrically induced, progressive improvement in responsiveness was noted after a lapse of time. This would suggest that the cells concerned may not have been permanently destroyed, but that as their functional activity returned so did consciousness.

All these conclusions as to the role of the reticular system in consciousness have been made as the result of animal experiment using cats and monkeys. It is noteworthy that the effects of lesions in the activating system of the animals with the higher degree of encephalization—the monkeys—were even more marked than the effects of similar lesions in cats. It would, nevertheless, be unjustifiable to draw conclusions regarding human behavior without evidence of human clinical material.

Depression of responsiveness, of reactive ability, and of purposive movement following vascular or traumatic interference with the human brain is a commonplace. This has been demonstrated by Kubik and Adams,[12] in 1946, and by Purdon Martin,[13] in 1949.

After work upon lesions of this sort, Dandy [14] considered the striate body to be the center of consciousness, a contention later contradicted by Meyers.[15]

Watson ‡ recently reviewed a number of cases of rupture of aneurysms in the neigh-

† References 9, 10.

‡ Watson, W. S. W.: Personal communication to the author.

borhood of the anterior communicating artery, and of lesions in the distribution of the basal perforating branches of the anterior cerebral artery at its origin. This was the area which Hughlings Jackson [16] thought might be associated with consciousness. It was found that such lesions, or indeed others at strategic levels of the diencephalon or brain stem, produced total loss or global impairment of consciousness, possibly through interference with the reticular system. Watson found that ruptured aneurysms of the vessels referred to produced global impairment of consciousness for varying periods of time. He concluded that this effect and the brain stem ischemia causing it were originally determined by stretch and spasm of the vessels at the time of aneurysmal rupture and were accentuated by local retraction and hypotension at operation. He remarked, however, that it was not clear what relationship this mechanism had to the reticular activating system.

An accurate assessment of the relatively short-term clinical effects of such lesions as Watson has reviewed is indeed difficult. It may be that the manifestations noted are not to be imputed directly to the brain stem ischemia, but, rather, to near or distant disturbances of cerebral function.

For this reason, evidence dependent upon more permanent clinical alterations of consciousness is of more value. It is such evidence that is rare.

As early as 1890 Mauthner postulated a sleep center in the brain stem. In 1904 it was noted by Gordon Holmes [17] that lesions in the area of the red nucleus produced drowsiness, and, again in 1920, Kinnear Wilson [18] observed that unconsciousness resulted from midbrain compression. Penfield,[19] in 1938, indicated that the area concerned with consciousness lay in the periaqueductal gray matter.

In 1941 Cairns, Oldfield, Pennybacker, and Whitteridge [20] published their case of a third ventricle cyst producing alterations in consciousness and behavior which they labeled "akinetic mutism." This case was published before attention became focused upon the reticular system. The authors agreed with Penfield's localization, but also implicated the hypothalamus as being responsible for a synthesis of external and internal sensory impressions, and thus for consciousness.

In 1942 Dempsey and Morison [21] found that stimulation of the midline thalamic nuclei, structures included in the reticular system, resulted in a diffuse, rather than localized, cortical activation.

As a result of study of his neurosurgical cases, Geoffrey Jefferson [22] observed in 1944 that injury to the brain stem produced what he called parasomnia.

In 1948 and 1951 Thompson and Nielsen,[23] and Thompson [24] postulated that the area of conjunction of hypothalamus, subthalamus, and mesencephalon is that responsible for background consciousness.

In 1952 French [25] reported three cases with injury to the cephalic part of the brain stem. All the patients showed hypokinesia and mutism; they were inert and appeared to be asleep. Unfortunately, however, all his cases had additional lesions in locations other than the brain stem. While the cases are therefore suggestive, they cannot be taken as conclusive evidence that conscious awareness is dependent upon the integrity of the brain stem and reticular system.

Michael Jefferson,[26] in 1952, also published an account of six cases, all of whom showed disturbances of consciousness in association with lesions of the brain stem. He cited three cases of suspected angioma, one of suspected basilar aneurysm, one of basilar artery aneurysm, and one in which the causative lesion was unknown. Since all the patients recovered, no autopsy confirmation of these diagnoses was available. While Jefferson suggests that interference with brain-stem function was the probable cause of the disturbances of consciousness noted in his cases, he also admits that this was no more than a speculation, requiring pathological proof.

In the same year Cairns [27] reviewed many cases of disturbances of crude consciousness. He showed that consciousness was affected by lesions anywhere in the brain stem, but went a step further by pointing out that the degree of unconsciousness and its physical concomitants, such as hyperventilation or pyrexia, varied with the site of the lesion, which could thus be localized. Jasper [28] had pointed out that the reticular system of the thalamus is more highly differentiated than the more caudal portions in its effect upon consciousness. Cairns concludes his paper by postulating a mechanism concerned with awareness in the neighborhood of the third ventricle and independent of the great ascending and descending tracts. He was unable to conclude that such a mechanism was located in the reticular system.

An account of this rare case, in which the diagnosis was verified pathologically, would seem, in spite of its singleness, to be a valid contribution to the consideration of the role of the reticular system and its effect upon consciousness. The case bears a remarkable resemblance to the one originally described by Cairns [20] and his associates. In addition, the account forms an interesting speculative basis for future work upon the part played by the reticular system in the production of psychotic stuporous states.

Report of Case

A woman aged 41. No relevant family or early history. Married a laborer at 18. She had eight children, all alive and well. She was a jolly, friendly, hard-working, house-proud, thrifty person with few interests outside her family and home. Her last child was born prematurely and precipitately, when she was 39. Nine months later she began to show certain abnormalities, which are enumerated below.

(*a*) Trance-like States: These were episodes during which the patient would, in the midst of household activities, suddenly become inert and unresponsive and as suddenly, about 10 minutes later, would resume where she had left off.

(*b*) Drop Seizures: Two to three months after the onset of the trance-like states she began to have seizures in which she would, without warning, fall suddenly to the ground, almost immediately getting up and appearing normal but with no explanation of what had occurred. These seizures increased in frequency until, within six or seven months of their onset, they were occurring every three or four days.

(*c*) Intermittent Personality Changes: At the same time as the drop seizures started, but in no other relation to them or to the trance states, the patient began to show intermittent changes in behavior, when she would become irritable and careless of her housework and family. Such alterations in behavior would last about 36 hours and occurred at intervals of a few days; before and after them she was her usual self.

(*d*) Memory Defects: Sixteen months after the development of the trance-like states the patient began to show lapses of memory in the performance of her household tasks, making many minor mistakes and becoming irritable when these were pointed out to her.

(*e*) Loss of Financial Acumen: About three months later she became progressively more unable to manage the household allowance and started to spend money indiscriminately.

(*f*) Further Continuous Personality Changes: Concurrently with the above change she began to be more continuously unpredictable and irritable and, for the first time, emotional.

(*g*) Visual Defect: About the same time as this alteration in personality occurred, it was noticed that the patient was having difficulty in seeing persons or objects on her right side.

(*h*) Right-Sided Paresis: Three months later she began to drag her right foot and started using her left hand instead of her right. She began to find difficulty in dressing herself.

(*i*) Major Epileptiform Seizures: Concurrently or slightly preceding the start of the paresis, the patient had her first major seizure, with tonic and clonic convulsions followed by heavy sleep. There were no premonitory signs or after-effects. The seizures took place with increasing frequency, until before admission up to five were occurring every day. These finally—two years after the start of the trance-like states which were the initial signs—led to her referral for neurosurgical assessment.

At examination she was apathetic and just rousable, opening her eyes when questioned but otherwise making no response. Positive findings were right homonymous hemianopia, right upper-motor-neuron facial weakness, and right-sided hypertonicity, with motor weakness more marked in the arm than in the leg. Plantar responses were extensor. The EEG suggested the possibility of an abscess or a rapidly growing tumor with predominant involvement of the left cerebral cortex. Left carotid angiography and CSF studies were negative. Ventriculography showed enlargement of the interpeduncular space and suggested the presence of an irregular tumor of the anterior portion of the third ventricle. An epidermoid

cyst was incompletely removed from this area three days after her admission. Postoperatively she remained apathetic but responsive to painful stimuli. She was admitted to the mental hospital 12 days after her operation. She was then quite immobile and mute. Her respirations were quiet and steady. Her eyes were open and deviated to the left, and absence of the right blink reflex was indicative of right-sided hemianopia. Her head was turned slightly to the left, and she showed slight right facial flattening; grasp reflexes were present but were slightly stronger on the left. Withdrawal reflexes to pinprick were present over the trunk, both legs, the arms, and the face. There was slight hypertonus of the right leg and arm. Plantar responses were extensor. She was able to obey the repeated command to put out her tongue, and she made occasional purposive movements with both arms.

She showed some pseudocatalepsy in that when her left arm was lifted it tended to remain in the position in which it had been put for a considerable time. She was incontinent of urine. She was propped up in bed; a pen was put into her hand, and it was explained to her that she was required to sign her name. She appeared to understand what was wanted, grasped the pen feebly, but succeeded only in making a few meaningless scratches on the paper. Similarly, she was unable to make a cross. An attempt to get her to make a cross with her left hand was also unsuccessful. Her expression, while neither alert nor changing, was not that of a stuporous patient. She seemed to be aware and to have some retention of affect. She did not respond to the voice by any change of expression; yet one felt that behind this external appearance there was a sentient human being. It was considered that the peculiar mental condition she exhibited bore a striking resemblance to the syndrome entitled akinetic mutism described by Cairns, Oldfield, Pannybacker, and Whitteridge,[20] and which has already been mentioned.

She remained in this state for about 10 days. She was able to get up about a month following admission. She was no longer hypokinetic and mute but remained dull, lethargic, and listless, with no memory for the past, little knowledge of the present, and no interest in the future. She displayed a global memory defect, perseverated, and began to steal from other patients. Gradually she became more and more unoccupied and lacking in spontaneity. She showed considerable emotional blunting. She was able, however, to answer questions fairly coherently. Four months after admission she began to have grand mal seizures, sometimes as many as three a day. She was by this time existing at a very primitive level. Her behavior and attitude at times approached those of akinesia and mutism, but she remained conscious and aware of her surroundings. She continued in this way until she died, of pneumonia, six and a half months following admission.

At autopsy (Figure) an infrafrontal epidermoid cyst presented at the base of the brain, obscuring it. This craniopharyngioma, arising from the remnants of Rathke's pouch, extended upward into the region of the third ventricle and hypothalamus. The greater part of the cavity of the third ventricle was obliterated, and the lesion extended as far forward as the undersurface of the anterior two-thirds of the corpus callosum. Posteriorly and inferiorly it lay in relation to the midbrain and pons. There was involvement of the optic tract posterior to the optic chiasma, with extension of this involvement to the left toward the internal capsule.

Tumor of reticular activating system.

Comment

The cortex has long been held to mediate consciousness. That this is wholly correct has been called in question by the experimental work of Magoun and others, who have postulated that the diffuse projection system of the brain stem may be responsible for crude consciousness or awareness. The integration of clinical material with this work has remained incomplete.

The case reported is that of a woman aged 41. During the two years preceding admission her cardinal signs were episodic disturbances of consciousness. An epidermoid cyst of the third ventricle was incompletely removed at operation. She lived for about seven months after this but toward the end of this period again showed a marked impairment of consciousness. At autopsy no herniation of the brain stem and no evidence of hydrocephalus or of pressure on the cortex was found. During life there was no indication that her symptoms were due to cerebral anoxia. All her symptoms must therefore have been due to the local effect of the tumor of the brain stem.

Attention is drawn to two noteworthy features of the case.

At the time of her admission to the mental hospital the patient was in a state of akinetic mutism closely approximating that of the famous case described by Cairns and associates.[20] Both cases showed gross fluctuating impairment of awareness or wakefulness and motor activity. There followed, in the present case, a considerable amelioration of the impairment of consciousness, an amelioration which persisted more or less unchanged until her death, although the remaining tumor must still have been enlarging. The akinesia and mutism are explainable in terms of postoperative cerebral edema, but the impairment of consciousness persisted too long after operation to be so accounted for—that these signs should not have returned later in the illness can only be ascribed to the presumption that the continuing growth of the tumor was taking place in such a direction as not to involve further brain stem destruction. There is, however, no satisfactory answer to this problem.

It was noted earlier that in animal experiments with electrically produced lesions in the brain stem, progressive improvement in awareness occurred after the lapse of varying periods of time. It was suggested that the cells concerned were not permanently destroyed, but that as their functional activity returned, so did the level of consciousness rise. This may be the explanation of the disappearance of akinesia and mutism characteristic of the postoperative course in this case, assuming a fluctuating accession and recession of the tumor growth.

There is another feature of the case which is still unsolved. For the two years preceding this patient's admission to a neurological unit, she showed as her cardinal signs transitory and episodic disturbances of consciousness which have been described as trance-like states. These appear to have been akin to fleeting episodes of akinetic mutism.

Transitory epileptiform attacks in cases of tumor of the cerebral cortex are common, and by their focal signs indicate the site of the tumor. The episodic alterations in consciousness which occurred in this case during the two preoperative years may be susceptible of a similar explanation.

The case reported was one of an epidermoid cyst affecting the rostral end of the brain stem. It was a destructive lesion of nerve tissue, and its principal effect was gross impairment of consciousness. It has been established by previous animal and clinical work that such signs as were predominant in this case need not have been produced by interference with the great ascending and descending tracts. Thus the presumption that disordered function of the reticular activating system was responsible is reasonable, although the mechanism remains unestablished.

It is now generally agreed that the maintenance of consciousness depends upon an

area and upon an unknown mechanism within the brain stem.

Cairns [27] has established that destructive lesions in the anterior part of the third ventricle produce, variously, stuporous states, fits of various types, including petit-mal-like fits, and in one case a condition resembling catatonic schizophrenia. The consideration that this has many possible implications with regard to psychotic stuporous states is very pertinent and gives rise to obvious speculation. The observation does establish that somewhere within the brain stem lies a mechanism intimately concerned with the maintenance of consciousness, a fact confirmed by the case reported here and by other clinical material which has been reviewed.

Summary

A brief description of the reticular system of the brain stem is given.

Some of the available experimental and clinical evidence that destructive lesions to the brain stem produce impairment of consciousness is reviewed, and it is concluded that this is probably due to interference with the brain-stem reticular system.

A single case of tumor is reported. The case was that of a destructive lesion involving the rostral end of the brain stem and producing gross impairment of consciousness as its cardinal sign.

It is accepted that no conclusions can be drawn from a single case, but it is confirmed and emphasized that destructive lesions to the brain stem produce states closely akin to many psychotic conditions in which alterations of consciousness are involved, and whose causation remains obscure.

The speculation is made, subject to further clinical observation of others, that certain psychotic states may be due to disturbances of the brain-stem reticular system.

REFERENCES

1. Schiller, F.: Consciousness Reconsidered, A. M. A. Arch. Neurol. & Psychiat. 67:199-227, 1952.

2. Clark, W. E. Le Gros, in Prospects in Psychiatric Research, edited by J. M. Tanner, Oxford, Blackwell Scientific Publications, 1953.

3. French, J. D.; von Amerongen, F. K., and Magoun, H. W.: Activating System in Brain Stem of Monkey, A. M. A. Arch. Neurol. & Psychiat. 68: 577-590, 1952.

4. Moruzzi, G., and Magoun, H. W.: Brain Stem Reticular Formation and Activation of EEG, Electroencephalog. & Clin. Neurophysiol. 1:455-473, 1949.

5. Starzl, T. E.; Taylor, C. W., and Magoun, H. W.: Ascending Conduction in Reticular Activating System with Special Reference to Diencephalon, J. Neurophysiol. 14:461-477, 1951.

6. Starzl, T. E.; Taylor, C. W., and Magoun, H. W.: Collateral Afferent Excitation of Reticular Formation of Brain Stem, J. Neurophysiol. 14:479-496, 1951.

7. Magoun, H. W.: Symposium on Brain and Mind: Ascending Reticular Activating System in Brain Stem, A. M. A. Arch. Neurol. & Psychiat. 67:145-154, 1952.

8. Ranson, S. W.: Somnolence Caused by Hypothalamic Lesions in Monkey, Arch. Neurol. & Psychiat. 41:1-23, 1939.

9. Lindsley, D. B.; Schreiner, L. H.; Knowles, W. B., and Magoun, H. W.: Behavioural and EEG Changes Following Chronic Brain Stem Lesions in Cat, Electroencephalog. & Clin. Neurophysiol. 2: 483-498, 1950.

10. Lindsley, D. B.: Bowden, J. W., and Magoun, H. W.: Effect upon EEG of Acute Injury to Brain Stem Activating System, Electroencephalog. & Clin. Neurophysiol. 1:475-486, 1949.

11. French, J. D., and Magoun, H. W.: Effects of Chronic Lesions in Central Cephalic Brain Stem of Monkeys, A. M. A. Arch. Neurol. & Psychiat. 68:591-604, 1952.

12. Kubik, C. S., and Adams, R. D.: Occlusion of Basilar Artery in Clinical and Pathological Study, Brain 69:6-121, 1946.

13. Martin, J. P.: Consciousness and Its Disturbances Considered from a Neurological Aspect (Lumleian Lecture), Lancet 1:1-6; 48-53, 1949.

14. Dandy, W. E.: Location of Conscious Center in Brain—Corpus Striatum, Bull. Johns Hopkins Hosp. 79:34-58, 1946.

15. Meyers, R.: Dandy's Striatal Theory of "Center of Consciousness": Surgical Evidence and Logical Analysis Indicating Its Improbability, A. M. A. Arch. Neurol. & Psychiat. 65:659-671, 1951.

16. Jackson, H., in Selected Writings, edited by J. Taylor, London, Hodder & Stroughton, 1931.

17. Holmes, G.: On Certain Tremors in Organic Cerebral Lesions, Brain 27:327-375, 1904.

18. Wilson, S. A. K.: On Decerebrate Rigidity in Man and the Occurrence of Toxic Fits, Brain 43:220, 1920.

19. Penfield, W.: Cerebral Cortex in Man: Cerebral Cortex and Consciousness (Harvey Lecture), Arch. Neurol. & Psychiat. 40:417-442, 1938.

20. Cairns, H.; Oldfield, R. C.; Pennybacker, J. B., and Whitteridge, D.: Akinetic Mutism with Epidermoid Cyst of Third Ventricle (with Report on Associated Disturbance of Brain Potentials), Brain 64:273-290, 1941.

21. Dempsey, E. W., and Morison, R. S.: Production of Rhythmically Recurrent Cortical Potentials After Localized Thalamic Stimulation, Am. J. Physiol. 135:293-300, 1942.

22. Jefferson, Geoffrey: Nature of Consciousness, Brit. M. J. 1:1-5, 1944.

23. Thompson, G. N., and Nielsen, J. M.: Area Essential to Consciousness—Cerebral Localization of Consciousness as Established by Neuropathologic Studies: Scientific Exhibit, J. A. M. A. 137: 285, 1948.

24. Thompson, G. N.: Cerebral Area Essential to Consciousness, Bull. Los Angeles Neurol. Soc. 16:311-334, 1951.

25. French, J. D.: Brain Lesions Associated with Prolonged Unconsciousness, A. M. A. Arch. Neurol. & Psychiat. 68:727-740, 1952.

26. Jefferson, M.: Altered Consciousness Associated with Brain Stem Lesions, Brain 75:55-67, 1952.

27. Cairns, H. W. B.: Disturbances of Consciousness with Lesions of Brain Stem and Diencephalon, Brain 75:109-146, 1952.

28. Jasper, H. H.; Ajmone-Marsan, C., and Stoll, J.: Corticofugal Projections to Brain Stem, A. M. A. Arch. Neurol. & Psychiat. 67:155-166, 1952.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

ASCENDING PATHWAYS OF THE TRIGEMINAL NERVE IN CAT. C. M. BERRY, F. D. ANDERSON, AND D. C. BROOKS, J. Neurophysiol. 19:144, (March) 1956.

Berry, Anderson, and Brooks report observations on the ascending trigeminal pathways studied electrophysiologically. The ventral secondary tract, composed of rapidly conducted potentials, was found along the contralateral medial lemniscus. A dorsal ascending pathway, consisting of rapidly conducted potentials, was found bilaterally just lateral to the medial longitudinal fasciculus. Both early and late potentials were found in the medial regions of the thalamus. Attempts to trace the continuity of an isolated pathway was limited by the diffuse distribution of potentials between the midbrain and the thalamus. Since rapidly conducted potentials appeared in the centrum medianum, it is suggested that the medially placed extralemniscal pathways are not exclusively "slow" with trigeminal nerve stimulation.

SIEKERT, Rochester, Minn.

COMPARATIVE HISTOLOGIC AND ELECTRON MICROSCOPE INVESTIGATIONS OF THE CENTRAL NERVOUS SYSTEM. L. ROIZIN and L. DMOCHOWSKI, J. Neuropath. & Exper. Neurol. 15:12 (Jan.) 1956.

Roizin and Dmochowski report extensive observations on the spinal cord of the guinea pig studied by means of the electron microscope. The tissues were treated with osmic acid. They noted distinctive morphologic aspects of the nucleolus, nucleus, and nuclear membrane and the complex structural organizations of the cytoplasm of neurons. The nucleolus consisted of a solid structure with irregular contours and no visible limiting membrane, and from it irregular strands extended into the nucleoplasm. The nucleus was composed principally of irregular clumps of dense particulate material scattered within a pale nucleoplasm. Nissl constituents, mitochondria, and opaque osmiophilic structures were seen commonly, and the Golgi apparatus and neurofilaments occasionally in the cytoplasm.

The glial elements consisted of a well-defined, centrally placed, oval nucleus with a dense single osmiophilic membrane, cellular body, and processes. Mitochondria were seen in the glial cytoplasm.

The myelin sheath appeared as a dense osmiophilic structure, laminated concentrically in certain instances. The oxoplasm of the nerve fibers disclosed a large number of neurofilaments.

SIEKERT, Rochester, Minn.

Physiology and Biochemistry

ALDOSTERONE IN CLINICAL MEDICINE—PAST, PRESENT, AND FUTURE. J. W. CONN, A. M. A. Arch. Int. Med. 97:135 (Feb.) 1956.

Conn reviews the historical background of the recent discovery and isolation of the new and potent electrolyte-regulating adrenocortical harmone, aldosterone. Both primary and secondary forms of hyperaldosteronism and hypoaldosteronism are described or hypothesized. Primary forms are classified as pure or mixed, depending upon whether over-all-adrenal stimulation/depression or specific aldosterone stimulation/depression is encountered. Secondary forms of hyperaldosteronism, as seen in various states associated with edema, nephrosis, congestive cardiac failure, etc.; or without edema, as seen in severe diaphoresis or dietary restriction of sodium, both pure and mixed, are described. The more obscure secondary hypoaldosteronism syndromes are suggested. Ten cases of primary hyperaldosteronism, in which the pathological substrate consisted of a adrenocortical tumor, are reviewed. All these cases exhibited hypokalemia, hypernatremia, and alkalosis, and of particular neurological interest were neuromuscular disturbances, such as tetany, periodic weakness, paresthesiae, along with other symptoms, such as polydipsia, polyuria, and arterial hypertension. The prompt disappearance of all the above-described symptoms following surgical removal of the cortical adenoma

suggests a definitive form of therapy for certain neuromuscular disorders, such as familial periodic paralysis in a certain number of instances, of which investigation may reveal this pathological defect.

PARSONS, Montrose, N. Y.

THE PREPARATIVE ISOLATION OF CEREBROSIDES. N. S. RADIN, J. R. BROWN, and F. B. LAVIN, J. Biol. Chem. 219:977 (April) 1956.

Starting with commercial cerebroside concentrate (24% pure), the material is extracted with ether and hot alcohol, processed chromatographically with Florisil to remove phosphatides, and passed through a column of mixed ion exchange resins, which yield, without recrystallization, cerebrosides 88% pure. After precipitation as a barium derivative, it is crystallized. A method for determination of galactose in cerebroside is presented.

PAGE, Cleveland.

COPPER CONTENT OF THE BRAIN AND LIVER IN HEPATIC ENCEPHALOPATHY. H. PORTER and R. D. ADAMS, J. Neuropath. & Exper. Neurol. 15:61. (Jan.) 1956.

Abnormalities of copper metabolism are a constant finding in hepatolenticular degeneration; the copper contents of the liver and of the brain and the amount of urinary excretion of copper are all increased. In hepatic encephalopathy or hepatic coma, the copper content of the liver, the urinary excretion of copper, and the levels of copper in the plasma may be increased. Porter and Adams analyzed the copper content of the putamen and of the liver in patients who died in hepatic coma (most commonly caused by alcoholic cirrhosis) and in suitable controls. The average copper content of the liver was noted to be increased, but not consistently. There was no significant difference in the copper content of the brain of those with hepatic coma and those serving as controls.

SIEKERT, Rochester, Minn.

ON THE MUSCULAR RIGIDITY AND HYPERREFLEXIA DUE TO HYPOTHERMIA IN MAN WITH OBSERVATIONS ON THE ACCOMMODATION OF PERIPHERAL NERVE. JOHN A. SIMPSON, J. Neurol. Neurosurg. & Psychiat. 18:191 (Aug.) 1955.

The clinical picture of progressive hypothermia is characterized by a progressive delay of cerebration, dysarthria, and a sluggish response of the pupils to light as the temperature is reduced below 80 F. An unusual feature is the retention of muscle tone and stretch reflexes during hypothermia.

Simpson reports a case of accidental hypothermia in a 77-year-old white man who was found in an unconscious state after having been exposed in an unheated room with a temperature of approximately 48 F for four days. Examination of the patient revealed a rectal temperature of 72.5 F, and there was increased resistance to all passive movements of the limbs. As the patient's body was gradually warmed by a radiant heat cage, he became more restless, and it became difficult to restrain the movements of his limbs. He remained comatose, and all muscle groups exhibited marked rigidity with greatly overactive tendon reflexes.

The nerve accommodation of the ulnar nerve in this hypothermic patient was found to be comparable to that in a patient with latent tetany. The diminished accommodation of peripheral nerve is usually accompanied by lowering of the rheobase and results in repetitive firing of motor units in response to a single stimulus to the axon, as in tetany. Simpson believes that this state is a major factor in the hyperreflexia of hypothermia and that the hypertonic state may be analogous to tetany.

MANDEL, Philadelphia.

HYPOPHYSECTOMY IN MAN. R. LUFT, H. OLIVECRONA, D. KORNERUP, and H. LJUNGGREN, Brit. M. J. 2:752 (Sept. 24) 1955.

In an attempt to arrest the progress of diabetic vascular complications, Luft and co-workers performed hypophysectomy on 20 patients between 20 and 33 years of age. The purpose of the operation was to eliminate those anterior pituitary factors shown to have a diabetogenic action. All patients had diabetic retinopathy, albuminuria, and proteinuria, and in most cases the blood pressure was elevated. Patients were observed for periods ranging from 3 to 43 months. Seven of the twenty patients died from 1 day to 19 months after operation. Substitution therapy consisted in administration of thyroxine, estrogens or androgens, and adrenocortical hormone.

Luft and co-workers realize that the therapeutic value of hypophysectomy for the vascular complications of diabetes cannot be determined on the basis of their small number of cases and the limited period of observation, but they consider the results obtained to be encouraging. In the patients who survived the operation, the blood pressure dropped and the heart volume decreased. Calcification of peripheral vessels was not affected by the operation, but calcification did not develop in the cases in which it was not present preoperatively. Capillary fragility was normal. The albuminuria and glomerular filtration rate definitely decreased, but there was no change in the effective renal plasma flow. There was no evidence of progression of renal disease or retinal changes, and visual capacity improved in some patients.

ECHOLS, New Orleans.

Neuropathology

STUDIES IN CEREBROVASCULAR DISEASE: VI. EXPERIMENTAL CEREBRAL INFARCTION. PETER D. MOYES, KHAHL WAKIM, GEORGE P. SAYRE, and CLARK H. MILLIKAN, Proc. Staff Meet. Mayo Clin. 30:620 (Dec. 28) 1955.

The authors report their attempts to produce cerebral infarction in dogs by the injection of five combinations of materials into the internal carotid artery in the neck. The topical use of combinations of thrombin and sodium morrhuate solutions alone or mixed with blood proved unsatisfactory, for when infarcts were produced, death occurred within 24 to 36 hours in many cases. The injection of 48-hour-old homologous blood clot resulted in a blood clot which filled the proximal parts of the middle cerebral artery and its branches. In some cases the posterior cerebral artery and the internal carotid artery were filled. The animals survived between 3 and 26 days after the injection of the homologous blood clot.

The use of homologous blood clot was considered best, for infarcts were produced in a majority of cases and there was a low mortality rate to permit clinical and pathologic study. This technique reproduced rather closely the mechanism of cerebral embolism, but not of cerebral thrombosis.

MANDEL, Philadelphia.

STUDIES IN CEREBROVASCULAR DISEASE: VII. EXPERIMENTAL PRODUCTION OF CEREBRAL INFARCTION BY INTRACAROTID INJECTION OF HOMOLOGOUS BLOOD CLOT. NORMAN C. HILL, CLARK H. MILLIKAN, KHALIL WAKIM, and GEORGE P. SAYRE, Proc. Staff Meet. Mayo Clin. 30:625 (Dec. 28) 1955.

The experimental production of cerebral infarcts in animals is important, since it may be of assistance in evaluating the high incidence of similar lesions in humans, in whom information on physiological and pathological changes is still lacking.

The authors used the intracarotid injection of 0.2 cc. of homologous blood clot in dogs and produced cerebral infarction in 20 of 25 animals (80%), with a mortality rate of 16%. The clinical signs could be correlated with the size and site of the infarct. Infarction of moderate size in the thalamostriate area, if associated with little or no cortical infarction, tended to produce mild signs. Infarcts of similar degree in the thalamostriate area, if associated with a greater degree of cortical infarction, resulted in severer signs. If the infarct of the thalamostriate area was large and cortical infarction occurred, the signs tended to be severe. Death occurred if there was extensive infarction in both thalamostriate and cortical areas and was usually associated with gross infarction in the white matter.

The site of the infarction was generally limited to the distribution of the middle cerebral artery. The gross appearance of the infarcts was variable, but the infarcts tended to be hemorrhagic. In the surviving animals, the amount of infarct which was hemorrhagic had no relation to the severity of the signs. In the animals that died, the contribution to the death of the animal of that portion of the infarct which was hemorrhagic could not be stated, although in three of the animals that died more hemorrhagic infarction was present than in any animal that survived.

The embolus could be identified in only 16 of 25 animals. In 14 cases the clot could be identified in the middle cerebral artery or one of its branches, but in 6 cases (30%) no clot was found near the area of infarction. The authors could not adequately explain this point but state that further study of this important point is indicated.

MANDEL, Philadelphia.

ALTERATIONS IN AUTONOMIC GANGLION CELLS IN FEVER, DEHYDRATION, AND INANITION. H. C. PRIBOR, A. M. A. Arch. Path. 61:91 (Jan.) 1956.

Pribor reports a study of the histological and histochemical changes produced in the autonomic ganglia of cats by artificially induced fever, dehydration, and starvation. The most constant morphological abnormality was shrinkage of the autonomic ganglion cells. The glycogen content of these cells, as determined by PAS stains before and after digestion with diastase, was diminished in all the animals. In those subjected to dehydration or starvation PAS-positive material resistant to digestion with diastase (and therefore probably not glycogen) was seen. The chromidial substance was increased in the febrile and in the rapidly dehydrated animals. Acid phosphatase activity of the ganglion cells was reduced in all three groups. The content of alkaline phosphatase was low in the three groups, but also in the controls. The Golgi apparatus underwent early hypertrophy, followed by progressive diminution in size in dehydrated and starved animals, but was rapidly reduced in size and fragmented in those with fever. The significance of these changes in relation to the metabolism and function of the ganglion cells is discussed.

APONTE, Philadelphia.

POLIOMYELITIS: XV. THE SPINAL CORD. A. B. BAKER and SAM CORNWELL, A. M. A. Arch. Path. 61:185 (March) 1956.

The entire spinal cord in each of 50 cases of fatal bulbar poliomyelitis was sectioned at all levels and prepared with hematoxylin and eosin, the Nissl stain, and Weil's stain. In all cases the changes in other parts of the nervous system were known. Meningeal involvement was present in over half the cases and was invariably associated with myelitis at the corresponding level, but did not match the severity of the latter. The commonest site of meningeal involvement was the region of the anterior commissure. In only six of eight cases showing definite thickening of the leptomeninges was this of sufficient severity to cause a mild degree of compression of the anterior roots, with subsequent demyelination of these fibers. Interstitial parenchymal inflammation of some degree was present in all cases, was always diffuse through the various levels, affected the cervical and thoracic portions most consistently, and was located most frequently in the anterior gray horns. Degenerative changes in the anterior-horn cells were most marked in the cervical level (96%) and involved the medial and lateral groups with about equal intensity; as the lower levels of the cord were approached, these changes became less pronounced. The mildest, and apparently reversible, form of anterior-horn-cell disease was acute swelling and diffuse perinuclear chromatolysis. The cells of the posterior horn were definitely damaged in only one case; those of Clarke's column, in two cases. Complete chromatolysis with nuclear fragmentation of internuncial cells was seen in 42 instances, at all levels, most prominently in the posteromarginal group. Areas of necrosis accompanied by intense inflammation and little glial reaction occurred in the anterior-horn cells of 13 cases; in two it was very extensive and involved the entire group of these cells, extending into the posterior horns.

An attempt was made to correlate morbid changes with clinical manifestations. Up to 18% of anterior-horn cells were seen to have been destroyed without apparent muscular weakness; when over 40% of them had been damaged, paralysis had been present during life. Damage to the internuncial cells did not appear to play an important role in producing muscular involvement. No correlation was found between pleocytosis of the spinal fluid and clinical or pathological findings.

APONTE, Philadelphia.

PRIMARY INTERCEREBRAL PLEOMORPHIC RETICULUM-CELL SARCOMA. E. J. LOSLI, A. M. A. Arch. Path. 61-322 (April) 1956.

The neoplasm described herein involved the left frontal lobe and head of the caudate nucleus of a 25-year-old white man. Admission to the hospital was precipitated by episodes of depression and confusion, unaccompanied at first by signs of organic brain disease. Electroencephalograms revealed "diffuse abnormality," and a pneumoencephalographic study disclosed marked displacement to the right and downward of the left anterior horn of the frontal lobe. The patient died 13 days after operation. At necropsy a firm tumor mass was found infiltrating diffusely the left caudate nucleus, thalamus, and cerebral penduncle, compressing the third ventricle, invading the mammillary bodies and, caudally, the medial aspect of the left temporal lobe. There was no evidence of neoplasm outside the brain. Microscopically, the tumor was unencapsulated and permeated diffusely the surrounding parenchyma. In the

better-preserved areas were seen large cells—some mononuclear; others multilobulated and multinucleated. There was considerable variation in size and shape of the tumor cells, and mitoses were abundant. Silver stains revealed a fine reticulum penetrating between and joining tumor cells. Although the multilobulated cells resembled Sternberg-Reed cells, the authors believe the lesion to represent a reticulum-cell sarcoma, rather than Hodgkin's disease.

APONTE, Philadelphia.

Psychiatry and Psychopathology

THE PERSONALITY OF POLIOMYELITIS PATIENTS WITH DISTURBANCE IN BLADDER FUNCTION. K. SIMMA, Monatsschr. Psychiat. u. Neurol. 131:177 (Feb.-March) 1956.

Simma reports a series of eight cases of acute anterior poliomyelitis occurring in young adults in which transitory urinary retention was a conspicuous feature, and one relatively poorly correlated with the degree of paralysis. The author reviews the physiological mechanisms of bladder function, stressing the role of sympathetic retention "centers" at L2-L4. Although pathological, the author stresses the fact that children with severe involvement of these "centers" fail to evidence the specific type of urinary problem (transitory retention) noted in these cases. On this basis, he asserts that the disturbance is to be interpreted as a manifestation of excessive sympathetic "tonus" brought about in persons of suitable personality structure (those having unresolved pubertal problems) as a response to an affliction with a dreaded illness, i. e., poliomyelitis. The author supports the above assumption by citing the infrequency of this particular stress reaction in prepubertal poliomyelitis victims and its occasional occurrence in physically healthy postpubertal persons with masturbatory anxiety problems.

PARSONS, Montrose, N. Y.

Meninges and Blood Vessels

EXCISION OF OCCLUSIVE LESIONS OF THE MIDDLE CEREBRAL ARTERY. KEASLEY WELCH, J. Neurosurg. 13:73 (Jan.) 1956.

Following an occlusion of the middle cerebral artery or one of its branches, important readjustments of the circulation may occur which may limit the area of destruction that results. Extensive softening is not the inevitable result in all instances, for in some cases, depending upon the efficiency of the collateral circulation, a complete recovery of function may occur even after a surgical closure of the middle cerebral artery. In more recent studies, other investigators have demonstrated that the meningeal-artery anastomoses with the terminal branches of the middle cerebral artery tend to protect the cortex from infarction in the distribution of the occluded vessel. The rapidity with which the collateral circulation is established is undoubtedly an important factor, and definite advantages would be expected if the obstruction was relieved and blood flow was reestablished.

Welch reports two cases of occlusive lesions of the middle cerebral artery in which the obstruction was surgically removed. In the first case, a 47-year-old man developed a left hemiplegia during sleep, and three weeks later, when he failed to improve with medical treatment, an arteriogram demonstrated an obstruction of the common right middle cerebral artery. A thrombus was removed, and the clinical recovery was good except for loss of finger dexterity. The second case was that of a 51-year-old woman who had auricular fibrillation, and 12 hours after the onset of a right hemiplegia an embolus was excised from the left middle cerebral artery. Her neurological status was unchanged, and subsequent arteriography revealed an obstruction of the middle cerebral artery as prior to surgery.

MANDEL, Philadelphia.

Diseases of the Brain

INFANTILE CORTICAL HYPEROSTOSIS. G. G. CAYLER and C. A. PETERSON, A. M. A. J. Dis. Child. 91:119 (Feb.) 1956.

Infantile cortical hyperostosis is a syndrome comprising cortical subperiosteal new-bone formation, commonly involving the mandible and the long bones, and usually associated with tender swelling of the involved area. Warmth and redness of the skin and lymphodenopathy are not seen. It is commonest during the first six months of life and appears to be self-limited and benign. The cause and specific treatment are unknown. The leucocyte count is

elevated; low-grade fever and anemia may occur. Roentgenograms disclose the hyperostosis. Rarely, swelling and pain are associated with weakness or paralysis of a limb.

SIEKERT, Rochester, Minn.

ELECTROENCEPHALOGRAM IN SUBDURAL HERMATOMA. H. A. KAPLAN, W. HUBER and J. BROWDER, J. Neuropath. & Exper. Neurol. 15:65 (Jan.) 1956.

The authors studied 30 patients harboring subdural hematoma collections and attempted to correlate the type of electrical activity with the symptomatology and physical findings before and after operation. The patients with the greatest clinical disturbances, including disturbance of the conscious state, were seen among those with the greatest degree of electroencephalographic abnormality. The type of electrical activity found preoperatively had no bearing on the rapidity of postoperative improvement, as determined either by clinical or by electrical observations.

The term "impeded effect" was coined to describe the appearance of wave forms frequently recorded from the affected side, and determined by lower amplitude, slower frequencies, and less sharply defined wave forms.

The authors believe that the type of electrical activity seen over subdural hematoma collections may be due to involvement of deep structures.

SIEKERT, Rochester, Minn.

OLIGODENDROGLIOMAS IN THE YOUNG AGE GROUP. S. W. BERKHEISER, J. Neurosurg. 13:170 (March) 1956.

Oligodendrogliomas are slow-growing tumors which usually involve the cerebral hemispheres of adults, but they rarely occur during the first and second decades of life. Berkheiser reports two cases which were found in children, the first occurring in the vicinity of the third ventricle in a 5-year-old child and the other in the frontal lobe of a 14-year-old girl. In each case there was a history of trauma that obscured the diagnosis.

The microscopic examination of the tumor tissue removed revealed small uniform cells with clear cytoplasm, a finding consistent with oligodendroglioma. In the case involving the frontal lobe, there were sheets of tumor cells within the subarachnoid space and invasion of the adjacent dura. Berkheiser states that subarachnoid seeding and dissemination are not unusual features of these tumors in children and adults.

MANDEL, Philadelphia.

TAY-SACHS DISEASE IN TWO SINHALESE CHILDREN. C. C. DE SILVA and G. E. TENNEKOON, Brit. M. J. 2:768 (Sept. 24) 1955.

The authors report two cases of Tay-Sachs disease in Sinhalese boys aged 30 months and 25 months, respectively. Until recently the infantile type of this disorder had been described almost exclusively in children of Jewish stock. Clinical manifestations included mental retardation; myoclonic fits; blindness, with a dark-purple patch at the fovea centralis surrounded by a white halo of avascular degenerated tissue, and primary optic atrophy. In one case the age of onset of the illness was 2 months and the duration 32 months; in the other these respective figures were 2 years and 2 months. The microscopic changes found were those usually described by others. The only unusual feature was the presence of large hyalin masses undergoing calcification in some parts of the brain substance and in the pia-arachnoid.

ECHOLS, New Orleans.

NEUROLOGIC MANIFESTATIONS OF NASOPHARYNGEAL TUMORS. H. E. ROSENBAUM and W. B. SEAMAN, Neurology 5:868 (Dec.) 1955.

Neurologic symptoms occur initially in 25% of nasopharyngeal tumors, and the nervous system is involved at some time in approximately 50% of cases. The frequent intracranial extension of these tumors is due to the fact that the majority of tumors arise from the fossa of Rosenmüller, which is in close proximity to the base of the skull, particularly the foramen lacerum and foramen ovale. The tumor extends intracranially through the foramen lacerum and comes in contact first with the abducens nerve, but may extend forward and involve the trigeminal, oculomotor, and trochlear nerves. The last four cranial nerves arise too far posteriorly to become involved intracranially, but they are frequently involved near the lateral nasopharyngeal wall. Horner's syndrome was also encountered in the authors' series, which was based upon an analysis of 24 patients who had neurologic symptoms as initial symptoms of nasopharyngeal tumors.

In these cases, the roentgenogram was characterized by the presence of a soft-tissue mass in the nasopharynx and destruction of the floor of the sella turcica. The free portion of the sella was intact, whereas the base and floor of the sella were destroyed. The submental-vertex, or base view of the skull, was one of the most valuable views taken to demonstrate the bony destruction which frequently occurred in nasopharyngeal tumors.

MANDEL, Philadelphia.

TUBEROUS SCLEROSIS WITH ACCOMPANYING SYMPTOMS OF PARANOID PSYCHOSIS. H. Z. WINNIK and M. ASSAEL, Monatsschr. Psychiat. u. Neurol. 131:151 (Feb.-March) 1956.

The authors report the case of a 23-year-old man having many of the typical symptoms of tuberous sclerosis, including skin changes and a state characterized by epileptic attacks of a psychomotor type (EEG normal) with interseizure periods of paranoid behavior. Medical treatment was unsuccessful in reducing the severity of the psychotic symptoms, but a marked improvement succeeded bilateral frontal leucotomy, after which the attacks, as well as the interseizure paranoid state, resolved.

PARSONS, Montrose, N. Y.

THE STURGE-WEBER SYNDROME. A. JUBA and G. ZETENY, Monatsschr. Psychiat. u. Neurol. 131:163 (Feb.-March) 1956.

Juba and Zeteny report two cases of the Dimitri-Sturge-Weber syndrome, one of which, a child of 10 years, demonstrated a capillary nevus in the trigeminal distribution, spastic hemiparesis, mental deficiency, and epileptic seizures, along with the finding of the characteristic configuration of intracerebral calcification by x-ray and a vascular malformation at operation. The second case, a 50-year old man, presented similar findings, with the exception of the facial nevus, which was absent, as well as the additional operative finding of a subdural lipoma overlying the characteristic vascular lesion. In the first case surgical intervention, with radical removal of the masses and adjacent pathological convolutions, was succeeded by significant cessation in the epileptic seizures and improvement in the mental state. The theory of a developmental defect involving mesenchymal differentiation of the intracranial contents in the causation of the syndrome is supported by the presence of the lipoma in relation to the lesions seen in the second case.

PARSONS, Montrose, N. Y.

PSEUDOTUMOR CEREBRI. JACK DUNN JR., GEORGE S. BAKER, and HENRY P. WAGNER, Proc. Staff Meet. Mayo Clin. 30:505 (Nov. 2) 1955.

Pseudotumor cerebri is a condition characterized by papilledema and increased intracranial pressure in which no demonstrable cause can be demonstrated. It occurs in younger patients, usually below 30 years of age, and abnormal neurologic signs are absent or minimal. The etiology of this condition has been attributed to an excessive production or diminished absorption of cerebrospinal fluid.

The authors report four cases in which edema of the brain occurred from water-electrolyte imbalance secondary to toxic, infectious, hormonal, or allergic factors. In each instance the patient responded dramatically to a conservative program consisting of the restriction of salts and fluids. They believe that pseudotumor cerebri is therefore the result of swelling of the brain in electrolyte imbalance. Dehydration therapy is indicated in order to preserve the patient's vision. Dural-sinus venography was not done in any of the cases, as the patients responded to the conservative measures.

MANDEL, Philadelphia.

Diseases of the Spinal Cord

CERVICAL MYELOPATHY. EDWIN CLARKE and J. H. LITTLE, Neurology 5:861 (Dec.) 1955.

Clarke and Little report the case of an 81-year-old woman who had a history of progressive weakness of the hands and shoulder girdles terminating in quadriplegia, with a sensory level at C3, nine weeks before death. Roentgenograms of the cervical spine revealed gross degenerative changes at all levels, particularly at C5-6, with slipping forward of the body of C2 upon C3. The spinous processes and laminae also appeared to be smaller than normal. The patient remained bedridden, became confused, and died as a result of congestive heart failure. At autopsy a sharply delineated compression of the posterior surface of the dura mater at the level of C2-C3 was encountered. This was caused by the laminae of C2,

together with the ligamentum flavum between it and the laminae of C3, protruding into the spinal canal. The dura mater was thickened at this level but not adherent. The laminae and spinous processes of C2 and C3 were found to be smaller than the remaining cervical vertebrae, a most unusual finding. There was also forward slipping of C2 upon C3 and the formation of a "step" between the posterior surfaces of these vertebrae, which projected posteriorly into the spinal cord to indent the anterior surface of the cord. The meninges were compressed at this point and were markedly thinned. Microscopic examination revealed complete demyelination of fibers at the level of compression. There was almost complete fiber loss in the region of the pyramidal tracts, whereas the posterior columns were less involved.

The authors believe that the congenital anomaly of the arch produced no signs or symptoms during most of her life; but, as the patient aged, degenerative changes occurred in the intervertebral discs and the potential instability of her spine became apparent, with the development of cervical spondylosis. The deformity between C2 and C3 appeared, and the cord damage ensued. The cord was damaged by anterior compression due to protrusion of the laminae and the ligamentum flavum.

The authors suggest that the spinal cord lesion was the result of cervical spondylosis, appearing in the presence of symptomless congenital smallness of the laminae and spinous processes of the axis. This may be one of the factors in the production of spondylotic myelopathy. They advocate more careful radiologic and pathologic study of the normal and diseased cervical spine to evaluate this theory.

MANDEL, Philadelphia.

EXPERIENCES WITH HIGH CERVICAL CHORDOTOMY. WILLIAM S. OGLE, LYLE A. FRENCH, and WILLIAM T. PEYTON, J. Neurosurg. 13:81 (Jan.) 1956.

The use of high cervical chordotomy for the relief of intractable pain has increased because of frequent unsatisfactory results obtained with high thoracic chordotomy and the technical difficulties encountered with mesencephalic tractotomy and medullary spinothalamic tractotomy. High cervical chordotomy offers the advantages of relatively few technical difficulties, sustained high levels of analgesia without islands of hypalgesia or sparing distal to the site of the cord incision, and a relatively low operative mortality rate. The procedure should be considered for surgical treatment of pain prior to physical debility and narcotic addiction.

In the authors' series of 81 chordotomies, paresis of the ipsilateral extremities occurred in 13 cases, being transient in 12 of these cases and not disabling in the other case. Urinary retention was found in 11 cases but was permanent in only 2 cases. In each of the 11 cases a bilateral chordotomy had been performed. Seven patients with amputation-stump pain and phantom-limb pain were treated with high cervical chordotomies. Four of these patients had complete relief of the pain, and the remaining three experienced some, but not complete, relief. The authors believe that amputation-stump pain can be relieved by high cervical chordotomy provided that the level of analgesia is high and no "islands" of sensation remain.

In this series, there were 11 (13.5%) postoperative deaths; with a more careful selection of patients and elimination of the erect position for the performance of bilateral chordotomy, the authors feel that this mortality rate could have been lessened.

MANDEL, Philadelphia.

EVALUATION OF ROUTINE SKULL FILMS IN INTRACRANIAL MENINGIOMAS. T. F. LEIGH, E. F. FINCHER, and M. F. HALL, Radiology 66:509 (April) 1955.

It has long been recognized that some abnormality will be found in plain films of the skull in approximately 50% of patients having meningiomas. A meningioma may produce one or more of the following positive findings in the routine roentgenographic examination of the skull: (1) bony alterations, either productive or destructive; (2) vascular alterations; (3) tumor calcifications; (4) sellar alterations; (5) pineal shift. The sellar alterations and pineal shift are not specific, since they may occur in any expanding intracranial lesion. The first three changes are fairly characteristic for meningioma.

Meningiomas are thought to originate in the villi of the pia-arachnoid. The villi extend into the dura, so that grossly the tumor appears to arise from the dura. The roentgenographic changes in the bone, appearing as osteoporosis, erosion, or hyperostosis, are all caused by infiltration of the tumor cells into the bone in the intertrabecular spaces and the Haversian canals. Ultimately new bone is laid down in the region of the invasion. Sometimes no tumor cells can be identified in hyperostotic bone; when a meningioma is removed and this hyperostotic bone is left in place, tumor growth within the bone apparently ceases.

The meningioma is a vascular tumor which often produces evidence of change in the vascular channels of the skull. Locally one often sees a network of fairly wide vascular channels or a fine honeycombing of the inner table of the skull. A meningioma may derive its blood supply wholly or in part from those vessels which normally groove the inner table of the cranial bones. Thus, it is not uncommon to see a large groove for the middle meningeal artery on the side of the tumor. The diploic veins may also be enlarged in the region of the meningioma. Roentgenograms show calcium deposits in about 20% of cases of meningiomas. The calcium is deposited within the psammoma bodies of the tumor and produces a typical punctate appearance.

WEILAND, Grove City, Pa.

SPINAL CORD INJURIES. JOSEPH P. EVANS and ADOLF ROSENAUER, A. M. A. Arch. Surg. 72:812 (May) 1956.

The records of 87 patients with spinal cord injuries who were treated by the senior author during the years 1937 to 1954 were surveyed. Fifty per cent of 43 patients with cervical cord injury died during hospitalization; 31% of 29 patients with thoracic cord injuries died, but all patients with cauda equina injuries survived. Of the 31 fatalities, 5 occurred within the first 24 hours; they were in part due to associated injuries. An additional 15 patients (11 with cervical and 4 with thoracic injuries) succumbed in the first week. The life expectancy increased considerably after the first week. The presence of a subarachnoid block proved to be no reliable criterion for laminectomy. On occasion, the presence of a manometric block was not substantiated by subsequent operation. There was no evidence that patients with a manometric block did better postoperatively than those without one.

It is customary to perform a laminectomy in order to remove foreign bodies, bone fragments, and acutely protruded discs or extradural hematoma. Another purpose of laminectomy is to decompress the swollen spinal cord and to relieve vascular embarrassment. In the authors' experience, protrusion of a disc or extradural hematoma is extremely rare in acute cord injuries. Edema of the spinal cord can be relieved only by incision of the pia, but this procedure appears inadvisable, since it causes protrusion of pulped cord tissue.

In summary, the authors take a pessimistic attitude. They feel that no clear-cut indications exist for laminectomy; furthermore, it remains uncertain whether or not the patient's chances are really improved by the decompressive operation (except for cauda equina lesions). The indication for laminectomy is frequently a psychologic one, to assure the patient and his relatives that everything possible has been done.

LIST, Grand Rapids, Mich.

A SURVEY OF THE NEUROLOGICAL RESULTS OF 858 SPINAL CORD INJURIES: A COMPARISON OF PATIENTS TREATED WITH AND WITHOUT LAMINECTOMY. A. E. COMANN and A. A. KAUFMAN, J. Neurosurg. 13:95 (Jan.) 1956.

The authors reviewed 858 cases of spinal cord injury in a Veterans Administration Hospital. These cases were evaluated from the standpoint of the effect of laminectomy in the various types of injuries encountered and the duration of injury to the time of laminectomy.

The laminectomized patients usually represented the most severely injured persons, and this type of surgical intervention was performed in 579 cases at various intervals after injury. Of this group, the results were better when no evidence of subarachnoid block existed. Sixteen per cent of the patients operated on were significantly improved, 8% were ambulatory—1.2% without aids. Of the patients not operated upon, 29% improved neurologically and 16% were ambulatory—6% without aids. Of importance in the surgically treated group seemed to be that the improvement following exploration was as frequently obtained and apparently as extensive in patients operated upon from a week to a month after injury as in those who had an early operation. The authors suggest that the acute paraplegic may profitably be treated with deliberation, not only to assess the need for intervention but to prepare the patient for it. Lower rates of improvement were observed in all types of lesions operated upon more than one month after injury.

In all patients, the intraspinal nerve lesions recovered more frequently than the spinal cord lesions. The least improvement occurred in injuries of the upper thoracic cord, and the greatest recovery followed lesions of the lumbar area. This indicated that trauma to the neural structures was tolerated better by the mobile cauda equina than by the less displaceable spinal cord.

The gross appearance of the spinal cord at operation was not always a reliable indication of the prognosis, for in some instances the cord appeared normal and the patient did not improve, whereas in other cases obvious subtotal lesions improved.

The authors conclude that if there is no doubt that the neural structures are completely destroyed, then laminectomy is not indicated. If there is doubt, and there is evidence of subarachnoid block, as well as roentgenographic evidence of bone injury, then surgery is indicated. If no subarachnoid block is present, conservative management is indicated.

MANDEL, Philadelphia.

Treatment, Neurosurgery

THE SURGICAL TREATMENT OF VERTIGO. SHOICHI HONJO and RYUZO FURUKAWA. A. M. A. Arch. Otolaryng. 63:153 (Feb.) 1956.

The surgical treatment of vertigo is limited to cases of unilateral labyrinthine involvement without preservable hearing in the affected ear. The indications for this type of treatment could be broadened if a method could be found to destroy the vestibular function, or enough of it, to eliminate the vertigo and at the same time preserve or improve the hearing.

The authors report two cases of vertigo which were of the unilateral type but had not responded to medical treatment. In the first case, coagulation of the labyrinth was performed, but the symptoms of tinnitus, deafness, and vertigo persisted. The second case was treated by exenteration of the ampullas of both the superior and the horizontal canals and the contents of the vestibule. The membranous structures in the vestibule and in both semicircular canals were ablated and destroyed as far as could be reached by forceps and dental excavators. In the second case the results were uniformly good, for the attacks of vertigo have been prevented and tinnitus has been relieved. Hearing was lost in this case.

The authors conclude that coagulation of the labyrinth fails to eliminate the vertigo but that more radical surgical destruction of the labyrinth by exenteration should be employed.

MANDEL, Philadelphia.

HYPOTHERMIA AND INTERRUPTION OF CAROTID, OR CAROTID AND VERTEBRAL CIRCULATION, IN THE SURGICAL MANAGEMENT OF INTRACRANIAL ANEURYSMS. E. H. BOTTERELL, W. M. LOUGHEED, J. W. SCOTT, and S. L. VANDEWATER, J. Neurosurg. 13:1 (Jan.) 1956.

The authors report the results of surgery in 22 patients at varying periods after rupture of an aneurysm, using a hypothermia technique to minimize the effects of anoxia. Hypothermia was induced in three stages. The first drop in temperature, of approximately 1.8 degrees (F), or 1 degree (C), resulted from preanesthesia medication, consisting of chlorpromazine, promethazine, meperidine (Demerol), and trichloroethylene anesthesia. The second stage occurred concomitantly with the cervical dissection, in which the patient's legs, groin, and lower abdomen were covered with crushed ice; and after the neck dissection was completed, the bath was filled with ice water and temperatures were checked until the rectal readings were at 86 F (30 C). During the course of the operation in the ruptured-aneurysm group, bilateral compression of the common carotid and vertebral arteries was found to be of value in 11 cases. The authors found that cerebral ischemia could be tolerated for a period of six minutes in the hypothermic patients with temperatures of 86 F (30 C), in contrast to three minutes of ischemia at normal temperatures. Ventricular fibrillation with death resulted in one instance as a result of the hypothermia. Death occurred in two other cases of ruptured aneurysms—one as a result of an associated intracerebral hematoma with ruptured aneurysm, and the second in a hypertensive diabetic patient with old softening in the distribution of the middle cerebral artery.

The electroencephalogram was used in all cases, for the appearance of delta activity was used as a guide to the maximum safe time for occlusion of the carotid or vertebral vessels in obtaining bloodless fields during the surgical approach to the aneurysm.

Of the 19 surviving patients the results in 16 were classified as good, in 1 as fair, and in 2 as poor. The authors believe that the combination of controlled hypothermia and reduction of cerebral blood flow by bilateral occlusion of the cervical vessels in varying combinations is of great help in the surgical approach to the treatment of ruptured aneurysms.

MANDEL, Philadelphia.

VALUE OF RADIATION THERAPY IN MANAGEMENT OF GLIOMA OF THE OPTIC NERVES AND CHIASM. J. M. TAVERAS, L. A. MOUNT, and E. H. WOOD, Radiology 66:518 (April) 1956.

Taveras, Mount and Wood studied the case histories of 34 patients thought to have primary glioma of the optic nerves and optic chiasm in order to evaluate the use of radiation therapy

and surgery in the management of these tumors. Of the 34 tumors, 19 were identified pathologically as piloid astrocytomas. In none of the other 15 cases was histologic examination of the tumor performed. In six patients the diagnosis was established by surgical gross inspection of the lesion without removal of tissue, and in nine cases the diagnosis was made by clinical and radiological methods alone.

The most constant radiological finding in glioma of the optic nerves is enlargement of one optic foramen. In a few cases both optic foramina are enlarged. Enlargement of one or both optic foramina was found in 26 patients. Pneumoencephalograms were performed in 21 cases, and in each case a suprasellar mass was demonstrated.

Optic nerve gliomas are tumors of young people. The average age of the 34 patients, when first seen, was 13 years; 15 were males and 19 females. Progressive visual impairment was a feature of all cases; those patients with normal visual acuity were usually found to have deficits in the visual fields. Symptoms of increased intracranial pressure were present in some cases. Increased pressure occurs if the tumor is large enough to block the foramen of Monro.

Surgery is indicated only for diagnosis or to relieve obstruction of the cerebrospinal fluid circulation. A possible exception is the tumor confined to one optic nerve, allowing complete surgical removal and destruction of the sight of one eye but no interference with the sight of the other eye. More frequently the tumor extends, at least partially, into the region of the optic chiasm, and in these cases radiation therapy alone is the treatment of choice. Taveras, Mount, and Wood found that radiation therapy often caused complete and permanent regression of an existing exophthalmos and often led to complete restoration of vision in an eye which was thought to be blind. Optic gliomas treated adequately with radiotherapy do not tend to recur. Radiation therapy, properly given, does not damage vital areas of the brain adjacent to the tumor.

WEILAND, Grove City, Pa.

Encephalography, Ventriculography, and Roentgenography

VERTEBRAL METASTASIS IN RENAL CARCINOMA. G. T. WOHL, Am. J. Roentgenol. 75:930 (May) 1956.

The occurrence of metastasis to the spine and pelvis from primary renal carcinoma is a fairly common occurrence. Between one-third and one-half of cases which have been studied show evidence of bone metastasis. The most frequent sites are the lumbar spine and the pelvis, but it is not uncommon for other bones to be involved. Wohl reports four cases of renal-cell carcinoma with metastasis to the spine. He believes that the intimate relation of the renal vein and its branches to the vertebral plexus of veins is responsible for the frequent metastasis to the spine. Renal carcinomas seem to have a tendency to invade the venous system and thus may readily pass both into the vertebral system and into the general venous return. Wohl was able to demonstrate the close association of the veins of the kidneys and the vertebrae by injecting contrast material into a vertebral body that was involved by metastasis in a living patient. Subsequent films showed that the contrast material had spread diffusely throughout this vertebral body and that there was a reflux of the contrast medium from the vertebral body through venous channels into the region of the superior pole of the left kidney. The left kidney was demonstrated to contain a tumor in subsequent studies.

WEILAND, Grove City, Pa.

Section on PSYCHIATRY

Behavioral Changes During Intracerebral Electrical Stimulation

JOHN W. HIGGINS, M.D., West Haven, Conn.
GEORGE F. MAHL, Ph.D.
JOSÉ M. R. DELGADO, M.D., New Haven, Conn.
and
HANNIBAL HAMLIN, M.D., Howard, R. I.

The aim of this paper is to describe the behavioral phenomena which occurred during electrical stimulation at various sites in the frontotemporal region * of the brain of an individual patient.

Much of the literature pertaining to problems of the neural correlates of behavior has recently been summarized and commented upon.[5] More specifically pertinent to this study were the demonstrations by various workers † of the correlations in animals between functions of the frontotemporal region and the expression of emotions and complex behavior related to feeding and sexual activity. Also, it has been demonstrated that "fear-like" reactions which could be elicited by stimulation of various areas in or related to this region had some properties of "real" emotions in that they entered into motivating and establishing learning.‡ The behavior experimentally elicited in animals seemed both complex and integrated. Consequently, there arose the question of whether and in what manner such behavior would be elicited in the human.

Some of the considerations involved in this question have been dealt with by Kubie.[6] Basing his ideas principally on Penfield's temporal lobe studies and MacLean's and Pribram's neuronography of the limbic system, he suggests that the frontotemporal region may represent a mechanism for the integration of perceptions and symbolic representations of the outside world with perceptions and symbolic representations of internal bodily processes. Our approach was couched in the form of relatively crude operational questions: Assuming any behavioral responses to electrical stimulation occurred, would they consist of reports of bodily or visceral sensations; would they be in the form of affective display, or would they be more complex, such as changes in ideation or changes in attitudes toward

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Assistant Clinical Professor of Psychiatry, Yale University School of Medicine; Neuropsychiatric Service, West Haven Veterans Administration Hospital, West Haven, Conn. (Dr. Higgins). Associate Professor of Psychology (Psychiatry), Yale University School of Medicine, New Haven, Conn. (Dr. Mahl). Associate Professor of Physiology and Psychiatry (Dr. Delgado). Consultant in Neurosurgery, State Hospital for Mental Diseases, Howard, R. I. (Dr. Hamlin).

* The frontotemporal region includes the posterior orbital, anterior insular, temporal polar, and periamygdaloid cortex.

† References 7 and 10.

‡ References 3 and 4.

others? Furthermore, would they be recognized by the patient; would they influence or be influenced by what could be understood to be the usual behavior of the patient?

I. The Patient

The patient was an 11-year-old boy with a four-and-a-half-year history of psychomotor epilepsy. From birth, he was alleged to have had an enormous appetite requiring breast and bottle feedings, from both of which he was weaned at 7 months. In infancy he was obese and "very active." At about 3½ years of age several events occurred: He had a tonsillectomy in a physician's office; his one sibling, a girl, was born; his father was admitted to a tuberculosis sanatorium, from which he rarely returned thereafter. By the age of 6 the boy had completed kindergarten and entered first grade, without remarkable event. When 6 years old, he fell ill with tuberculous meningitis. After the usual difficult course, he began to recover. During convalescence, he became increasingly hyperactive and began to show for the first time marked aggressive and destructive behavior. Within a few months, he began also to have seizures, occurring from four times a day to one every two months. These usually lasted about two minutes and consisted of diminution of awareness, pallor, retching, and vomiting, followed by confusion. His general aggressive behavior necessitated institutionalization at the Emma Pendleton Bradley Home. There, he socialized poorly.

Three years before this investigation, a Wechsler-Bellevue Intelligence Scale gave a Performance I.Q. of 110 and a Verbal I.Q. of 97. There was no evidence of impairment due to organic process; rather, there was impairment due to anxiety. The Draw-A-Person and Rorschach tests were administered. Comments about the data from these were: "He reacted to others by very active and hostile fantasy, resulting in fright and breakdown of ego control, followed by impulsive behavior, diffusely directed toward both sexes—There was somewhat greater tendency toward female identification. Repression and denial constituted major defenses." Two years later, the TAT and Draw-A-Person, Bender, and Rorschach tests were done. It was thought that he demonstrated "greater ego strength" and that there was a slight suggestion of the influence of organic processes. There also seemed to be evidence of "some masculine strivings." During institutionalization, the external controls and individual attention had relatively little effect. The response of the seizures to various analeptics was unsatisfactory. EEG tracings, repeated over a three-year period, showed abnormal activity at the left temporal region.

On these grounds, an amputation of the tip of the left temporal lobe was proposed by one of us (H. H.). In connection with this, it was planned to make use of the implanted electrode technique for diagnostic, and perhaps for therapeutic, purposes (J. D.). The aim was to attempt to determine the extent and location of abnormal areas, including examination of the possibility of bilateral abnormality. If a focus was found, an electrocoagulation of the affected site would be done via the electrode; if this failed, or the abnormal area was too extensive, it was hoped that the region for operative removal might be better defined; if bilateral foci were found, no operation of any kind would be advised. In order to proceed properly, explorations and electrical recordings would be carried on for several days. This provision would also allow the effects of anesthesia to pass.

II. Methods and Materials

A. Neurophysiological Methods.—The method of Delgado was followed, whereby electrographic tracings could be taken from, and stimulating or electrolytic currents passed through, each lead of the same four implanted multilead electrodes. This technique has been described elsewhere,§ but the pertinent details are given here. One needle electrode and one plate electrode were manually inserted through a temporal burr hole on each side. Each needle is approximately 12 cm. long (50 mm. being in the brain substance) and 0.5 mm. in diameter; it contains seven leads, which end at the tip 8 mm. apart and which protrude externally to a socket. Each plate electrode, made of polyethylene, is approximately 12 cm. long and also contains seven leads, the ends of which are 5 mm. apart and which extend externally to the socket.

Location of Electrodes: As verified by roentgenogram (Fig. 1), the tip of the left needle electrode was below the superior edge of the orbit and behind the anterior limits of the middle fossa, corresponding approximately to the superior part of the temporal lobe. One month after electrode implantation the tip of the left temporal lobe was removed, showing the electrocoagulated area in white matter of the superior temporal convolution.

The right needle was probably in the inferolateral part of the frontal lobe, and the plate electrodes overlay the cortex of the inferolateral frontal lobe on each side. (Figure 2 illustrates the numbering of the leads and suggests the position of needles and plates with respect to one another.)

§ References 1 and 2.

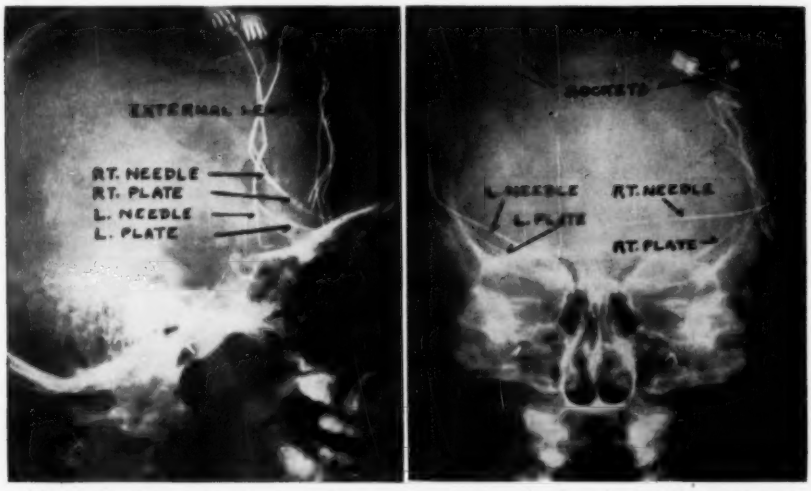

Fig. 1.—Lateral and anteroposterior roentgenograms showing implanted electrodes.

Electrographic Tracings: EEG tracings were taken continuously during the observation situations, except at the exact moments of stimulation or coagulation. (A Grass eight-channel electroencephalograph, Model III-B, was used.) Bipolar recordings were made, usually of adjacent pairs of points. At chosen times, oscilloscope tracings were also obtained. (A study of the electrical activity of the frontotemporal area in this and in seven other patients will be presented elsewhere.)

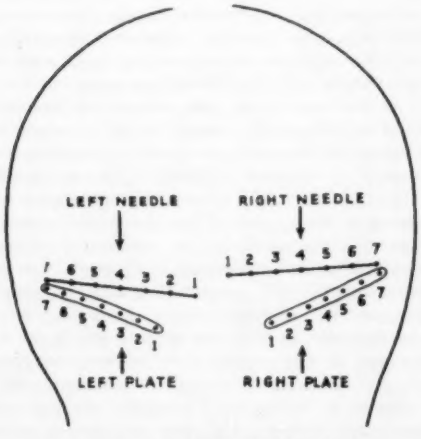

Fig. 2.—Schematized drawing of electrodes to illustrate the Points *5, 6,* and *7* on the *Needle* are relatively close to similarly numbered points on the *Plate,* and that points *1* and *2* on the two are widely divergent.

Stimulation: Stimuli were applied with a Grass Stimulator (Model S-4, with an isolation unit) set to deliver unidirectional stimuli with a pulse duration of 0.5 msec. and a frequency of 100 cps. They were applied for five seconds, ordinarily through adjacent points. The usual practice was to apply a certain number of stimulations at a given voltage and then to apply several at different voltages. The stimuli ranged from 3-12 volts and from 0.7-3.5 ma.‖

Coagulations: Coagulations at three points were the last procedure performed. With the constant-current instrument constructed by Mauro and Delgado, a direct current of about 6 ma. was passed through the desired point for about 90 seconds, with the positive as the active electrode.

B. Psychological Method.—Our interest was in the vicissitudes of sensory experiences, ideas, affects, and motivations. An interview situation was selected as the method most likely to offer a continuous supply of data. Specifically it was thought that a question-answer method might be less likely to produce the desired flow and quality of data, and therefore less valid. The behavior to be observed included the physiognomic display, and especially the language behavior. Each interview was tape-recorded and a typed transcript

‖ The Grass Stimulator isolation unit had a different output impedance on the 15-volt than on the 150-volt scales. True voltages as monitored with the oscilloscope during stimulation did not correspond with dial readings. For example, 15 volts, at the low-scale reading, and 50 volts, in the high-scale reading, both corresponded to 12 volts in the oscilloscope. The corrected figures are used in the report.

TABLE 1.—*General Nature and Sequences of Interviews*

Interview	Length of Interview, Min.	Number of Stimulations	Condition of Interview and Observations Made
1	40	0	3 hr. preoperative Recorded interview
2	38	0	1 day postoperative and after implantation of electrodes Recorded interview
3	100	14	2d postoperative day Recorded interview Depth EEG recording
3-a	90	20	2d postoperative day Recorded observation period Depth EEG recording
4	88	16	6th postoperative day Recorded interview Depth EEG recording
5	142	19	6th postoperative day Recorded interview Depth EEG recordings Coagulation of selected areas
6	50	0	12th postoperative day 6th day after removal of electrodes Recorded interview

prepared. Written notes were made of the observable physical behavior. In all, six interviews were carried out, with an additional observation period. The general identification and sequence of these interviews are presented in Table 1.

Plan of the Interviews: The first, second, and sixth interviews were for the purpose of gathering data for comparison with the stimulation interviews. During the latter, the interviewer and the patient had no knowledge of the times or sites of the stimulations, all of the electrical recording and other equipment being in another room, with the other investigators. One of the collaborators (G. F. M.) monitored the interviews in order to observe the apparent gross effects of stimulation and to inform another (J.D.) of suitable times for stimulation. Consequently, at that time, one of the observers who participated in the later interview analysis was exposed to knowledge of the times and sites of stimulation. However, he did not convey this information to the interviewer and did not refer again to his notes during the four-month period in which the interview analysis was taking place. His memory as to times of stimulation turned out to be faulty. The timing of the stimulations depended on two factors: the disappearance of any EEG changes following a previous stimulation, and the decision of the monitor, who tried to select times when the patient was being quiet.

At the time of the first stimulation interview (and of Observation Period 3-a), it should be emphasized that we were novices concerning the quality of behavior expected upon stimulation. Therefore, for these sessions the only factor influencing the pattern of the stimulation schedule was the neurophysiological exploration. There was little or no consideration of "controls" for the psychological observations. Following the above sessions, the neurophysiologist decided to leave the electrodes in place for another five days. As a result, it was possible to plan further psychological observations, using a more systematic schedule of stimulation. Basically, the plan for Interviews 4 and 5 consisted of selecting seven sites for stimulation at the same intensity which would provide a survey of the available areas. The sequence was such that in Interview 4 the seven sites would be gone through in rotation and then stimulated a second time with the order

reversed. (By technical error, two unplanned sites were also introduced.) This was to be repeated in Interview 5. The major purpose of this order was to control for sequence effects. In addition, during the fifth interview, an on-the-spot decision was made by the monitor to request repeat stimulations of three sites when the prearranged schedule was complete. This decision was based on a judgment of the striking nature of the material during the scheduled stimulation at the sites. The diagnostic and therapeutic aims of the procedure did not allow time for repeat stimulations of the other tested sites, nor was there time for examination of all other available areas. In all, 12 different sites were stimulated in Interviews 3, 4, and 5 and 3 additional sites in Interview 3-a.

The plan of the sixth interview was to explore further some of the behavior seen in the stimulation interviews. Consequently, the latter half of it was more directive than the other interviews.

Analysis of Interview Data: The analysis of the interviews consisted of a clinical-anecdotal appraisal and an objective evaluation. The clinical descriptions reflect the consensus impressions of two observers (J. H. and G. F. M.) of significant events and of the vicissitudes of the patient-interviewer interaction. The summaries are based on repeated study of the recordings.

In the objective evaluation, the purpose was to allow quantitative statements without contamination by preconceptions of the effects of stimulation. Manifest patient content and behavioral categories were judged independently by the two observers upon listening to the recordings and reading the transcripts. The unit of behavior categorized was that behavior of the patient occurring (*a*) between two successive interviewer comments, (*b*) between five or more seconds of silence, if such occurred, or (*c*) between such silences and a comment by the interviewer. In all, there were 39 categories. Some of these were formulated on the basis of the "live" interview observations, preliminary listening to the tapes, and initial tentative clinical formulations. Others were added as the objective survey progressed. In such instances, all of the preceding material was replayed to judge independently the applicability of the new category. The categories were neither mutually exclusive nor exhaustive. Thus, a given unit could be placed in no category at all, in one category, or in more than one category. The categories were "tailor-made" to reflect what were regarded clinically as significant aspects of the patient's behavior. The complete list of categories is not presented or illustrated here. Those important for the present purposes are introduced later (Tables 6 and 7).

The independent judgments were collated in order to determine the reliability of the various categories and to identify for later quantitative descriptions those patient remarks which both observers had placed in any given category. All of the quantitative statements, and those about "significant" events, in the paper refer only to such independently agreed-upon judgments. For all of the categories cited there was significantly greater-than-chance agreement between the observers.

General verbal activity measures were also made for both patient and the interviewer in all interviews. This measure consisted of the number of seconds spent talking by either in successive two-minute intervals. The method used is highly reliable, repeat activity graphs by the same observer being almost identical.¶

During the interviews when stimulations were being applied, two tape recorders were used. One recorded the regular interview proceedings. The input of the second contained a dual microphone system which could be switched from a pick-up of the interview to one of the observers (J. D.), who at the appropriate times registered such information as changes of leads and times and sites of stimulation. Only the nonannotated recording was used in the study of the interviews. After the clinical and objective analyses of all interviews were completed, the second tape was played and information about stimulation was introduced into the typescripts. By using common cues in the two tapes, the exact time of occurrence of stimulation in relation to the interview events was obtained.

III. Results

The interviews are first considered individually. For each, there is a descriptive commentary containing both qualitative and quantitative information. In order to depict the context, the findings for the stimulation interviews will be discussed mainly in terms of "stimulation interval." This is the time interval from the beginning of one stimulation to the onset of the next one. Finally, there is a general summary of the interview findings.

INTERVIEW 1 (Preoperative; no EEG tracings).—Throughout, the patient was excited and hyperactive. His opening remark, "Are you going to kill me?" was said elatedly, as were most of his other comments. The interview was roughly divisible into three phases.

In the first, he seemed to be mainly concerned with exploring the situation. This

¶ Mr. Jon Eklund made these graphs.

was literally so in that he darted about examining various objects, many of which he put in his mouth, including the microphone. He frequently asked if he could have things: clamps, wires, bits of string, etc. These requests led up to a direct question about what he was going to be told, by which he implied a question about what was in the offing, since he had not had the situation wholly explained to him. When a definite reply was not given, he abruptly demanded something to eat. These demands continued until he was given some crackers. As he ate, there occurred one of his rare quiet periods. At this time, he answered a few questions about his own experiences and about his mother. The period of quietude passed with the disappearance of the crackers. He again became elated, in the midst of which he said to the male interviewer, "You-s-seem-seem like a beautiful nurse."

Following this, when he was told about the impending operation, the second phase of the interview started. This was characterized by playful, aggressive activity. First, he made a "joke": "I'm crazy; you're nuts. I eat the chicken, and you eat the guts." In this excited time, he also said such things as "you smell like perfume on you—you look cute." Following this, the playful aggressiveness increased. The patient sniffed, licked, kissed, and bit the interviewer. He was briefly quiet while he demanded more food; but when the requests were not granted, another, more prolonged and accentuated period of hyperactivity ensued. His physical contacts were more openly erotic, including forceful copulatory movements as he knelt on the interviewer's lap: "You make me *feel* like something." The verbal content was often confused but included profuse sexually toned remarks which, together with his behavior, seemed to imply confusion about his and the interviewer's sexual role: "I love nurses more than I love doctors—They have cute faces—than you—they're so cute. A doctor don't have a girl's face. A doctor don't wear lipstick and have a pretty nice face and perfume." This behavior came to an end when the interviewer finally restrained the patient.

Phase 3 was introduced with a reintensification of demands for food, following which he left the room to make similar demands outside. These were more openly aggressive: "Gimme something to eat, please; I'm starvin'. I'll eat this machine—please gimme somethin' to eat or else I'll kill you—I'm starved—I'll eat you up." He scuffled about with various people, never making a serious effort to stay out of contact. When promised more food, he returned to the room, and on request told a story about a girl and boy getting married. Some further random conversation led up to a statement of concern lest his grandparents die, following which he left the room and would not return.

The overt oral and sexual aspects of behavior in this interview were the most striking elements. These are reflected in the specific behavioral-category judgments (the "requests" and "confusion of sexual identity of others" categories). Later, Table 6 will show the percentage of his comments judged as falling in these categories in this interview.

In the afternoon following the first interview, the electrodes were inserted through bilateral burr holes, which were made with the patient under general barbiturate anesthesia.

INTERVIEW 2 (first postoperative day; no EEG tracings; no stimulations).—The patient appeared somnolent and depressed. This state was thought to be largely due to effects of the anesthesia and operative procedure. Throughout, the manifest verbal content and physical activity were in several ways the direct opposite of those described in the first interview. Whereas in the first he was predominantly hyperactive, here he was mainly hypoactive. He never inserted anything into his mouth. He made no effort to gain physical contact beyond the minimal offered by the interviewer, except for one time, when he bent over and nuzzled his

head in the interviewer's lap. The major verbal and physical behavior concerned his head discomfort and his desire to return to his room. At the outset he had been quietly friendly. When it became evident that his request for relief of discomfort was not to be granted, he reemphasized his complaints, his fatigue, and his desire to go to his own room. He responded minimally to attempts to force the conversation, looking away uninterestedly and falling silent for long stretches. The one positive response came when compassion was expressed to him for his distress of the previous day at the time of the operation.

The most striking behavior of this session is reflected in the percentage of his responses judged "rejecting statements" (Table 6).

INTERVIEW 3 (second postoperative day; depth EEG tracings; stimulations).—Fourteen stimulations were applied, seven of which were RP1-2. Their sequence, voltages, and spacing appear on Figure 3. The average length of the stimulation interval was 5 minutes 12 seconds, the range being from 2 minutes 45 seconds to 13 minutes 54 seconds. The major features of this interview were changes in the character and degree of the patient's communicativeness. A kind of base line, to which these changes might be referred, was a similarity in his general behavior to that seen in the second interview, that is, an attitude of restricted verbal communication, with occasional active turning away, and a principal verbal content of complaints of discomfort and plaintive demands to return to his hospital room. For the first five minutes, he was rather talkative in the latter vein. During the next 10 minutes, this content continued, but the amount of talking itself decreased. Throughout this period, and subsequent similar periods, the interviewer attempted to foster a friendlier, more spontaneous attitude by reacting compassionately, by urging, joking, and reassuring about possible fear, and by using any material offered. These overtures never produced more than single responses, and often not that.

In contrast, there were six instances of change from this basic situation, when there were sharp rises in the amount of talking, plus an attitude of increased friendliness. Each of these instances of friendly communication followed within 40 seconds after stimulation of RP1-2. The only time when stimulation at RP1-2 was not followed by

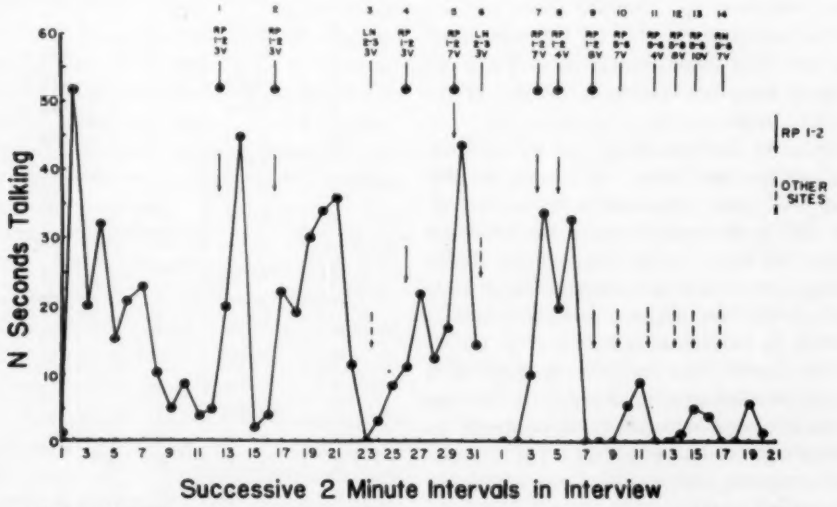

Fig. 3 (Interview 3).—Verbal activity of patient. Number (*N*) of seconds of talking in two-minute intervals.

TABLE 2.—*Differential Effect of RP1-2 and All Other Stimulations on Verbal Activity and Frequency of Friendly Remarks in Interview 3*

Stimulations	RP1-2 (N-7)		*t*-Test *P*-Value	All Others Stimulations (N-7)		*t*-Test *P*-Value
Time interval	2′ Prestim.	2′ Poststim.		2′ Prestim.	2′ Poststim.	
Mean % friendly remarks	6	53	0.02	17	10	--*
Mean N words by patient	17	88	<0.01	4	9	0.15
Mean N words by Int.	43	46	--*	16	30	>0.20

* Insignificant by inspection.

this behavior was the last at this site, when the voltage was changed. Characteristically, the rises were rapid, but brief and without any uniformity of verbal content. These changes in verbal activity are reflected graphically in Figure 3. Each of the rises following stimulation also showed an increase in the percentage of patient remarks judged "friendly verbalizations." The results of a quantitative analysis of these observations are shown in Table 2. The number of words spoken by the patient and the percentage of his "friendly remarks" were compared in the two-minute intervals preceding and following stimulation. The significances of the differences was determined by the *t*-test. Both the verbal activity and the frequency of "friendly remarks" increase significantly after RP1-2 stimulation but not after other stimulations. These increases were not due to a change in the verbal activity of the interviewer.

It can be concluded only that RP1-2 stimulations had this effect. It cannot be held that other sites stimulated at the same voltage and at the same times in the interview would not have had the same effect. These changes were not consistently found after any of the stimulations, including that at RP1-2, in Interviews 4 and 5.

The observations were not correlated with electroencephalographic change. At one time in the interview seizure activity occurred, together with a clinical seizure. The stimulation preceding this was at a site where five subsequent stimulations produced no seizure activity.

OBSERVATION PERIOD 3-a (evening of second postoperative day; EEG; stimulations).—After the first stimulation interview, just described, it was decided to stimulate several of the sites on the right side. An observer other than the usual interviewer, and not otherwise involved in this report, chatted amicably with the patient. Since there was no monitor, and because the patient-interviewer situation was different, the same kind of analysis has not

TABLE 3.—*Schedule of Stimulations and Dèjà-Vu Responses in Observation Period 3-A*

Stimulation			Reports of Dèjà-vu Experience
No.	Site	Voltage	
1	RN2-3	7	Déjà vu
2	RN2-3	7	Déjà vu
3	RN2-3	7	Déjà vu
4	RN2-3	7	Déjà vu
5	RN2-3	7	Déjà vu
6	RN4-5	7	Déjà vu
7	RN4-5	7	--
8	RN4-5	7	Déjà vu
9	RP6-7	7	--
10	RP6-7	7	--
11	RN1-2	7	Déjà vu
12	RN1-2	7	Déjà vu
13	RN1-2	7	Déjà vu
14	RP1-2	7	--
15	RP1-2	7	--
16	RP3-4	7	--
17	RP3-4	12	--
18	RP5-6	12	--
19	RP5-6	12	--
20	RN2-3	7	Déjà vu

been made of the exchanges. Nevertheless, the findings of this session are introduced because of the striking appearance of reported déjà-vu phenomena.

The stimulation schedule is given in Table 3. Of 12 stimulations at right needle sites, all but 1 was followed by a report of a déjà-vu phenomenon. Such reports occurred at no other times. Each of these responses had certain similar characteristics which are exemplified in one of the responses. At the time of Stimulation 3 (S3), the patient and observer were chatting about the auras preceding past attacks; the observer then asked a specific question about them. The patient began a reply, but stopped and said "I was thinkin'—it felt like someone else was asking me that before." Each déjà vu was a similar reference to a remark of either the patient or the observer which had been made just before, just after, or at the time that the stimulation was applied. They were reported immediately after stimulation, except that he would occasionally finish a previously begun statement first. He clearly perceived these thoughts as intrusive, although not disturbing. With many of the later ones, he would begin: "Hey—I had another strike. I had a feelin' . . . etc." The content always referred to whatever conversational theme was being pursued. Repeat stimulations of the same sites did not produce remarks of similar ideational content. The apparent affect was one of interested surprise. Stimulations of sites other than in the right-needle area caused no interruption in the conversation.

In Interviews 3, 4, and 5, no déjà vu response appeared following stimulation at sites other than in the right-needle area. One such response occurred in Interview 4 after RN2-3 stimulation. Of 22 stimulations at right-needle sites in Interviews 3, 4, and 5 and Observation Period 3-a, 12 were followed by this response, characteristically at deeper sites. The significance of these comparisons is shown in the following χ^2 analysis:

Stimulation Sites	Déjà Vu	
	Absent	Present
Right needle	10	12
All other sites	47	0
$\chi^2=27.6$	$P<0.001$	

Right-needle stimulation evoked the déjà-vu responses predominantly, but not exclusively, in Session 3-a. While the right-plate stimulation in Session 3-a did not evoke the response, we cannot state that stimulation of the remaining electrode sites on the left would not have done so. Nor can it be stated that stimulation of unexplored areas, in any interview, would not have done so. We can only conclude from our data that in this patient déjà-vu phenomena were a result of right-needle stimulation and that this effect was predominant in Session 3-a. The "interview difference" and the limiting considerations about area specificity are also pointed out for other categories and remarked upon in "Comment."

INTERVIEW 4 (sixth postoperative day; depth EEG tracings; stimulations).—Sixteen stimulations were applied in a prearranged sequence, with the exception of the sites of S1, S10, and S12, which represent technical errors. The sequence, voltage, and approximate spacing are shown in Table 4. The average length of the stimulation intervals was 3 minutes 54 seconds, the range being 2 minutes 44 seconds to 5 minutes 50 seconds.

The patient's conversation was disjointed, with fairly frequent silences. During some of these, he looked thoughtful; upon being asked, he would sometimes relate his thoughts, and sometimes not. The most consistent and pervasive aspect of his behavior was his attitude of friendliness and passive compliance, which note was struck from the beginning of the interview. Even during the silences, he tended to appear more animated and "in touch" than in Interview 3. The interviewer maintained an air of interest throughout, usually initiating no conversation. The exceptions were his questions about the patient's thoughts during most silences, and occasional attempts to allay anxiety, which he inferred to be

TABLE 4.—*Descriptive Summary of Stimulations and Significant Categories in Stimulation and Nonstimulation Intervals*

Interview 4

Interval No.	Stimulation Site	Voltage	Interval Duration, Min.	Significant Category*
0	Prestim.	--	26	Con
1	RN6-LP1	7	5	Con
2	RP1-2	7	4	----
3	RP6-7	7	4	Con
4	RN2-3	7	3	----
5	RN5-6	7	4	----
6	LP1-2	7	3	----
7	LP5-6	7	4	Pass com
8	LN5-6	7	2	Pass com
9	LN5-6	7	3	(1) Con; (2) osen
10	RP1-LN6	7	2	Con
11	LP1-2	7	5	Pass com
12	RP1-LN6	7	6	Pass com
13	RN6-7	7	6	(1) Osen; (2) pass com
14	RN2-3	7	3	(1) Déjà vu; (2) pass com
15	RP6-7	7	4	(1) Con; (2) pass com
16	RP1-2	7	4	(1) Con; (2) pass com

* "Con" indicates confused remarks; "pass com," passive compliance remarks; "osen," oral sensations.

present. There was no discernible correlation between his activity and the patient's language behavior, noted below. In this setting, there occurred several striking varieties of verbal communication, as follows:

1. Confused remarks about "the first word" and "so many people in the world." A typical example, which occurred before any stimulations, follows: (P) "Listen—if I say f'you the first word I says in my whole life, I would be a lit'—a big wrong. It'll be a big big wrong. Then if I ever says I —the first word now——." (T) "What's the first word?" (P) "One—that's the first word I talked." Such comments were sprinkled throughout. Since they occurred very noticeably even before stimulations, their appearance following stimulation (RN6-LP1; RP6-7; LN5-6; RP1-LN6; RP6-7; RP1-2) cannot be well evaluated. The message being conveyed by them remains in doubt.

2. Verbalizations of passive compliance (which were statements avowing his pleasure at being "up here" and subject to us). The first of these open declarations appeared precipitously following S7 (LP5-6). Having been silent during the previous five minutes, he said, "Hey! You can keep me longer here when you give me these; I like those." He went on to insist "they" make him "feel O.K." By "these" and "they" he meant "brain wave" tests. Subsequent similar statements followed S8, S11,

S12, S13, S14, S15, and S16. Later in the interview, these were coupled with expressions of fondness for the interviewer. The last one of the interview was accompanied by a voluptuous stretch. They did not appear in the first 26 minutes, when no stimulations were being applied, or in the 22 minutes preceding S7, when six other sites were stimulated. It was striking that he so suddenly expressed in words an attitude which had been previously present only in his nonverbal behavior. The difference between the frequency of passive compliance remarks before stimulations and the frequency after the onset of stimulations is statistically significant, $P<0.001$, as contrasted by χ^2 analysis.

This response category is regarded as a function of stimulation, but not of any particular site. However, it should be noted here that the initial appearance of this category of behavior was after the first stimulation at the site where, as will be shown, stimulation in the fifth interview was followed by verbalization of feminine sexual strivings. In addition, such statements were occasionally associated with emphatic expressions of "feeling good." The "interview difference" in the appearance of this behavior is also notable: It was not correlated with stimulation in Interview 5 and appeared not at all in the other stimulation sessions.

3. Reports of mouth sensations. A sensation of taste was reported following the second stimulation at LN5-6 (S9) but not following the first stimulation at this site. Mouth pain was reported following the one stimulation at RN6-7 (S13). These sensations were simply and barely reported and did not lead to an active verbal interchange, as did the phenomena described under (2). The correlation with stimulation will be commented on in the summary of Interview 5.

4. A déjà-vu-like response. This appeared after S14 at RN2-3, but there was no similar behavior when this point was first stimulated (S4). This remark was introduced in the context of a short conversation about his listening to other patients on his ward. He appeared struck by a thought and spontaneously reported: "—a feeling—I was thinking about somethin' somebody else was saying something like that once."

After stimulation at five sites (one time each at RP1-2, RN5-6, and RN6-7 and two times at RP6-7) electrical seizure activity from two to four seconds at sites near the point of stimulation were seen. On three occasions (following stimulation at RN6-LP1, RP1-2, LP5-6) slow waves appeared for three to four seconds, once in all leads and twice near the focus of stimulation. No motor or psychological concomitants were observed in connection with these, nor was there any consistent relationship to the above-described behavior.

INTERVIEW 5 (sixth postoperative day; depth stimulations; EEG tracings).—Nineteen stimulations were applied. The first 14 were by prearranged schedule; the last 5 were repetitions, based on "on-the-spot" decision, and were at a different voltage than the first group. The sequence, voltages, and approximate spacing are shown in Table 5. The last column of Table 5 is headed "Significant Category." This gives only the information that one or more of the behavioral categories was adjudged present in at least one response in the stimulation interval. It does not reflect how many responses were so rated. Because about 20 minutes elapsed after S19 until the coagulations were begun, this interval was conservatively cut off for analysis at two minutes. The average length of the stimulation intervals was 4 minutes, the range being 3 minutes 11 seconds to 8 minutes 16 seconds.

This interview was separated by only one hour from Interview 4, which it resembled in general tone. There continued to be fluctuations in the verbal activity, with the silences tending to be longer and more frequent than the silences in Interview 4. Again, the patient's usual attitude was one of passive compliance. The interviewer's behavior was generally the same as in the

TABLE 5.—*Descriptive Summary of Stimulations and Significant Categories in Stimulation and Nonstimulation Intervals*

Interview 5

Interval No.	Stimulation Site	Voltage	Interval Duration, Min.	Significant Category*
0	Prestim.	--	10	(1) Con; (2) pass com; (3) sexma
1	RP1-2	7	4	----
2	RP6-7	7	3	Con
3	RN2-3	7	3	----
4	RN5-6	7	3	----
5	LP1-2	7	4	(1) Sexma; (2) pass com
6	LP5-6	7	4	Sexma
7	LN5-6	7	4	Sexfem
8	LN5-6	7	3	Con (question of "being alive")
9	LP5-6	7	4	(1) Osen; (2) "alive"
10	LP1-2	7	3	----
11	RN5-6	7	5	----
12	RN2-3	7	3	(1) Con; (2) sexma
13	RP6-7	7	4	Osen
14	RP1-2	7	8	Con
15	LP5-6	4	8	(1) Osen; (2) sexfem
16	LN5-6	4	6	(1) Pass com; (2) sexfem
17	RN2-3	4	2	(1) Pass com; (2) sexma
18	LP5-6	8	14	(1) Osen; (2) sexma; (3) pass com; (4) con
19	LN5-6	2	2	(1) Osen; (2) "alive"
20	Poststim.	--	18	(1) Osen; (2) con; (3) pass com

* "Con" indicates confused remarks; "pass com," passive compliance remarks; "osen," oral sensation; "sexma," masculine strivings, and "sexfem," feminine strivings.

fourth interview. The findings of principal interest concerned the verbal content categories, especially under (3), discussed below. The verbal content of this interview can be substantially divided as follows:

1. Comments and questions about the numbers of weeks in a year, seconds in a week, seconds in a year, etc. (These had much the same quality as the "first word" comments of Interview 4 and were similarly scored "confused remarks.") They occurred before stimulations and in the intervals after S2 and S14, and late after the last stimulation, all of which were at different sites. Their relation to the times and sites of stimulation seemed in no way

consistent, and no attempt was made to check them by further stimulations. Their psychological significance remained unclear to us.

2. Verbalizations of passive compliance or avowals of pleasure at being "up here," similar to those described in Interview 4. They appeared in the intervals after S5, S16, S17, and S18, all of which were at different sites. However, the bulk of them occurred before the first stimulation and late after the last stimulation. A correlation with stimulations was not apparent.

3. Remarks judged to be concerned with feminine sexual strivings or confusion about own sexual identity. They occurred only in the intervals after S7 (LN5-6), S15 (LP5-6), and S16 (LN5-6).

Covert feminine strivings had been inferred from the material of the first interview. However, there were no verbal references to such strivings until the following occurred: At 1 minute 48 seconds after S6 (LP5-6) of this interview, he suddenly began to discuss his desire to get married. When asked "to whom," he did not immediately reply. During the silence, S7 (LN5-6) occurred. After being thoughtfully silent for 1 minute 20 seconds more, he said: "I was thinking—there's—I was saying *this* to you. How to spell 'yes'—y-e-s. I mean y-o-s. No! 'You' ain't y-e-o. It's this. Y-o-u." The topic was then completely dropped. The monitor (listening outside the room) took this to be a thinly veiled expression of a wish to marry the interviewer. Consequently, he asked that when the prearranged schedule was completed, these same sites be restimulated. In the intervening 40 minutes between S7 and S15, the patient spoke only of other things. Following S15 (LP5-6), a reference by the patient to facial hair (of the interviewer) led him to remarks about pubic hair and his having been the object of genital sexual play in the past, and then to an expressed doubt about his sexual identity: "I was thinkin' if I was a boy or a girl—which one I'd like to be." Following S16 (LN5-6), he remarked with evident pleasure "You're doin' it now," and then said "I'd like to be a girl." The sequel to these statements, which are the verbalizations after S17 and S18, are discussed in the next section.

More or less intuitively, the general passivity of behavior and open verbalizations of pleasurable passive feelings in Interview 4 had been formulated as linked to the feminine strivings. It was therefore striking when the first open expression of pleasure at passivity turned out to occur after stimulation at the same points in Interview 4 as those which in Interview 5 were followed by the open expression of feminine strivings. It cannot be concluded that the eliciting of this behavior was restricted to stimulations at LP5-6 and LN5-6. In the first place, only a few of the potentially innumerable areas of the brain where stimulation might yield such a response were tested during our observations. Second, except for one time, no other sites were stimulated at the different voltage of the repetitions at these.

(*a*) The following tabulation summarizes the frequency with which these verbalizations occurred in the intervals after LN5-6 and LP5-6 stimulations, and their frequency after the other stimulations when Interviews 4 and 5 are conservatively considered together.

As can be seen, the occurrence of such verbalizations is significantly associated with LN5-6 and LP5-6 stimulations. (The rationale for considering the two points together is their anatomic proximity, as indicated in Figure 2.)

(*b*) The appearance of verbalizations of

Intervals After Stimulation at	Verbalizations of Feminine Strivings	
	Absent	Present
LN5-6 and LP5-6	8	3
All other sites	24	0
	(By Fisher's exact test, P=0.02)	

feminine strivings was correctly predicted by the monitor during the course of Interview 5, when he specifically requested the repeat stimulations at these sites for further expression of them. Again, an "interview difference" in the appearance of these responses seems present, although the voltage differences in Interviews 4 and 5 prevent definite evaluation.

4. Responses judged to be concerned with "masculine" strivings. One of these statements occurred before S1 and one after S5 (LP1-2). They referred simply to aspirations toward adult "masculine" occupations and were not particularly striking. One occurred after S12 (RN2-3) and was a reference to being a grandfather and having children in the future. It was striking enough to provoke the monitor to request a later repetition (S17). The response was a remark making a favorable comparison of himself to a heroic prototype of "masculinity"—"Superman." The appearance of such a thought following upon his open remarks about wanting to be a girl seemed understandable on purely psychodynamic defensive grounds, the relation to stimulation being only incidental. The statements in the following interval after S18 (LP5-6) were urgent expressions of his desire to marry a "beautiful nurse." These seemed similarly understandable on psychodynamic grounds alone.

5. Questions about "being alive" at certain times in the future or past, which occurred in the intervals after S8, S9, and S19. The first and last of these were at LN5-6 and the second at LP5-6. These were characterized by an obtrusive introduction, brief exchange of remarks about them, and abrupt disappearance. They were such statements as "Will I be alive when I'm 100?" or "Will I be alive when it's 20-something?" Their psychological meaning is unclarified. When the type of statistical analysis just presented for "feminine strivings" is repeated for the "alive" statements, the same contingency table is applicable and the same significance result is obtained.

6. Reports of sensations. (*a*) Mouth sensations. Pain of an undefined nature, except for a reference once to a "broken tooth," was reported following S9 and S18 (both LP5-6) and S19 (LN5-6). An undefined smell was reported following S15 (LP5-6). His tongue "felt different" following S13 (RP6-7). All of the foregoing responses occurred within two minutes after stimulation. In addition, 19 minutes after S19 he spontaneously reported a pain in his mouth. Each of these sensations was simply reported and did not give rise to conversation about them, even when the interviewer tried to elicit it. These ***reports*** followed within two minutes of 7 of the 35 stimulations in Interviews 4 and 5. The suddenness of onset of these reports upon stimulation was notable. But, since an additional sudden report was given some 19 minutes after the last stimulation in Interview 5, this could not be readily regarded as a result of stimulation. Therefore, a statistical evaluation of the correlation between stimulation and all reports of oral sensations was made. The analysis consists of comparing the frequency of reports of oral sensations in the 35 two-minute intervals following stimulation with the frequency of such reports in all the remaining two-minute intervals in Interviews 4 and 5. The resulting contingency table and χ^2 test follow:

Stimulation	Report of Oral Sensations Absent	Present
2 min. interval	28	7
Control 2 min. interval	65	1

$\chi^2=8.1$; $P<0.01$

Additional note is taken of the characteristics of the stimulation sites where these responses appeared. The sites were RN6-7 and RP6-7, and LN5-6 and LP5-6. In each lobe, these paired sites were anatomically close to one another. Again, the "interview difference" is apparent: These reports were not elicited in Interview 3 or Session 3-a. However, the fact that stimulation at any

of these same four sites occurred only twice disallows further elaboration.

(*b*) Other bodily sensations were never reported as such, but one seemingly related phenomenon seems worthy of comment. Following S16 (LN5-6), just before saying "I'd like to be a girl," he remarked in a sensual manner, "You're doin' it now," as though he had had a pleasurable experience.

When the stimulations of this interview were completed, preparation was made to electrocoagulate those points which the electrophysiological data indicated were at or near the focus of abnormal activity. The interview situation was in effect at an end, since two other investigators had to enter the room to handle the required apparatus and because the sites and times of coagulation were audibly announced. The patient continued to talk a bit during the coagulations. There was content about dying and about being killed, following the first (partial) ablation (at LN5) and the second ablation (at LN4); this was expressed in a slightly elated manner. Verbalizations following the fourth ablation, at LN5, referred to a feeling of "being exploded"; this was directly followed by a fit. He looked fearful, became tachypneic, retched, and said nothing.

INTERVIEW 6 (12th postoperative day; electrodes removed).—The goal of this interview was to evaluate the status of some of the fantasies and ideas expressed in the stimulation interviews, especially those connected with feminine sexual strivings. To this end, the interview was intentionally structured into three phases: (1) a period of spontaneous recall, in which the opportunity was to be given to bring up whatever material he would; (2) a period in which he would be asked indirectly about his previous behavior, especially about verbalizations of feminine strivings, and (3) a period of direct confrontation about this and other material that had been elicited by stimulations but was not expressed in the preceding phases of this interview.

1. The period of spontaneous recall lasted for the first nine minutes. During this time, he talked about the "fun" he was having in the hospital, how he wasn't afraid, and how much "better" he felt. As he chatted, he seemed slightly elated and strolled playfully about the room. Although he effected only a minimal direct interchange with the interviewer, he was friendly. He did not refer to any details of the stimulation interviews, except for one reference to having "liked the brain waves." At no time did he express a desire "to be a girl."

2. The period of indirect questioning (lasting 12½ minutes) was begun when he was asked what he could recall about the previous talks. He referred to (1) a song which he had sung in Interview 3 and one from Interview 1; (2) "telling stories" about the boy-and-girl theme of Interview 1; (3) telling about his spells and previous hospitalizations. When he was pressed (but without specific reference) for more details of the stimulation interviews (identified to him by description of the situation), he changed the subject. After this, he played about some more and referred to the first interview. Shortly, he announced he was ready to return to his room, but he was persuaded to stay, with the presentation of gifts. He talked about the toys, strolled out of the room and returned, but made no further comments about the interviews.

3. The period of direct confrontation (which lasted 19 minutes) began when he was specifically reminded by the interviewer of his remarks in the fifth interview about "being married." He first spoke of the song in the first interview about a boy and a girl getting married. He then made up a song about Higgins and Mahl getting married, became excited, and wanted to leave. He denied being able to recall wanting to marry the interviewer but went on to ask if he had said "y-o-u" in response to a question about whom he wanted to marry. He denied that he had meant this; rather, he had meant that he was joking,

and then proceeded insistently to talk about his wish to marry a certain girl.

The interviewer asked if he remembered talking about wanting to be a "boy." The patient replied that he recalled having expressed a wish to be a girl, but immediately said that he didn't want to be one. Conversation about this led up to a declaration of wanting to be a man, although in the past he thought he might have been undecided about this. Doubt about this notion was expressed by the interviewer, to which the patient responded by saying *"sometimes* I'd like to have a *girl's face."* He then displayed a clay elephant he had been modeling for the past few minutes, referring specifically to the trunk, indicating that it would be "funny" to "squirt all over Dr. Mahl." Shortly, he ran vigorously out of the room, playing as if to squirt the monitor. He loudly insisted on remaining out, but the interviewer brought him back and asked about the "funny feelings" of the other interviews. This was answered by recall of some of the déjà-vu experiences of Period 3-a. When he continued in this vein, it was suggested that he was mentioning them only out of a desire to be pleasing. The patient became aggressive, elated, and excited, left the room, and did not return. He then played around in a very aggressive and hostile manner outside the interview room.

Summary of Interviews

A. Stimulation Interview Findings.—Of the observations cited in the previous descriptive material, the following behavioral categories are regarded as consequences of stimulation.

TABLE 6.—*Percentage of Patient Remarks Placed in Various Categories by Both Observers in Six Interviews, Reliability of the Judgments, and Significance Level of the Interview Differences by Categories*

Category	Interview						Reliability of Judgments		Significance Interview Diff.
	1	2	3	4	5	6	χ^2 Test *P*-Value	r_p	χ^2 Test *P*-Value
Requests or demands	18.9	7.7	1.7	3.6	0.9	2.2	<0.001	+0.76	<0.001
Rejecting statements	0	23.5	11.7	0	0	5.5	<0.001	+0.92	<0.001
Friendly verbalizations	0.4	0	17.8	23.0	29.6	16.6	<0.001	+0.46	<0.001
Verbalizations of passive compliance	0	0	0	10.2	0.9	0.7	<0.001	+0.67	<0.001
Verbalization of feminine strivings and confusion of own sex	0.4	0	0	0	3.8	1.8	<0.001	+0.80	<0.001
Verbalizations of masculine strivings	2.2	0	0	0	0.9	1.8	<0.001	+0.65	0.05
Verbalizations of confusion of sexual identity of others	4.1	0	0	0	0	0.4	<0.001	+0.84	<0.001
Confused remarks	4.1	4.5	4.1	8.4	8.5	3.2	<0.001	+0.63	0.02
No. of patient remarks	269	221	287	334	423	277			

1. Déjà-vu-like phenomena
2 and 3. Increased quantity and friendliness of verbalizations
4. Verbalizations of passive compliance
5. Oral sensations
6. Verbalizations of feminine sexual strivings
7. Verbalizations about "being alive" at certain dates

B. Interview Differences.—In the preceding descriptions of the individual interviews, reference has been made to the differences among them in respect to behavioral categories. Table 6 provides an over-all survey of the quantitative differences in the interviews in eight behavioral categories. These differences reflected the major clinical impressions. In the Table is shown the percentage of patient remarks placed in the content categories by both judges. As previously mentioned, each patient remark was judged according to whether or not one or more of these categories (and others unlisted here) was applicable. Also shown in Table 6 are the reliabilities of the judgments for the categories, all of which were significantly better than chance, although the interobserver correlations would have to be improved for more sensitive comparisons than are involved in this paper. The statistical significance of the differences in the various categories from interview to interview is also shown in Table 6.# This latter point will be further commented on in the final discussion. Table 7 summarizes the number of times oral sensations, déjà-vu experiences, and the "alive"-content category occurred in the interviews.

TABLE 7.—*Number of Oral Sensations, Déjà-Vu Experiences, and "Alive" Remarks in Interviews*

Category	Interview						
	1	2	3	3-a	4	5	6
Oral sensations	0	0	0	0	2	6	0
Déjà vu	0	0	0	11	1	0	0
"Alive" remarks	0	0	0	0	0	3	0

C. Stimulation Site Findings.—The particular effectiveness of stimulations at LN5-6 and LP5-6 in eliciting "significant" phenomena deserves special note. "Significant" refers to behavior that was striking in itself, was unusual even for this patient, and apparently occurred only upon stimulation. Table 8 is a rearrangement of some of the data to show which categories appeared and in how many intervals after stimulations at various sites in Interviews 4 and 5. (For example, of the four times LP1-2 was stimulated, verbalizations of passive compliance appeared in two of the stimulation intervals and verbalization of masculine striving in one. Since the categories are not mutually exclusive, only two intervals need be involved for these. The total of any one column in Table 7 does not indicate the number of different intervals showing the significant categories. One can meaningfully summate across the rows, but not down the columns.)

The verbalizations of feminine sexual strivings and questions about "being alive" appeared only in the intervals following stimulations at LP5-6 or LN5-6; five of the seven reports of oral sensations were in these intervals; the first appearance of verbalizations of passive compliance was after stimulation at these sites. However, it may be that stimulation of the other sites (or other completely untested areas) at different intensities would demonstrate a comparable efficacy.

IV. Comment

The data allow a conclusion that in this patient stimulation of various areas of the frontotemporal region evoked a range of

For three of the categories in Table 6—"masculine strivings," "feminine strivings," and "confusion over the sexual identity of others"—the theoretical frequencies used in the χ^2 analyses were quite small. The corresponding significance levels must be interpreted cautiously. The correction for continuity was used in all of the tests, including these three categories; so the *P*-values are to some extent conservative. Exact probability tests were not used for these categories because they are much too cumbersome for the gains achieved. It is unlikely that the *P*-values for the "feminine striving" and "sexual confusion" categories would shrink to insignificance in exact tests. Since the *P*-value of the "masculine striving" category might well do so, it should be viewed with suspicion.

TABLE 8.—*Number of Stimulation Intervals in Which Significant Categories Occurred in Interviews 4 and 5*

	RP1-2	RP6-7	RN2-3	RN5-6	RN6-7	LP1-2	LP5-6	LN5-6	RN6-LP1	RP1-LN6	Totals
No. of intervals	4	4	5	3	1	4	5	6	1	2	35
Confused remarks	2	3	1					1	1	1	9
Passive compliance	1	1	2		1	2	2	2		1	12
Oral sensations		1			1		3	2			7
Déjà vu			1								1
Masculine strivings			2			1	2				5
Feminine strivings							1	2			3
"Alive" remarks							1	2			3

manifest responses extending from direct sensory experiences to changes in complex behavior patterns. For the sake of discussion, it is possible to conceptualize a continuum, at one end of which are phenomena perceived by the patient as intrusive and foreign, or ego-alien; at the other are phenomena which do not seem to be so perceived. In the first class are the mouth sensations, which he reported in much the way he might have if a peripheral nerve had been stimulated. The déjà-vu phenomena, although obviously more complex, were responded to in much the same way, that is, as extraneous perceptions. On the other hand, the verbalizations of passive compliance were not spoken with any indication that he was aware of a foreign thought. They were voiced as reflections of his own feeling state. His statements about "feeling good" in connection with some of these statements may have represented perceived sensations, but even these were not reported as "foreign" events. Similarly, the verbalizations relating to feminine strivings had none of the quality of "forced thoughts." Except for their sudden and isolated appearance, they were spoken with the same confiding and reflective attitude more customarily heard in a psychotherapeutic session. In certain respects, the increases in verbal activity and friendliness of verbalization were more striking instances of totally integrated behavior, since it is highly unlikely that he was even aware that he was behaving in this way.

The second conclusion is that in this patient there was a tendency toward area differences in the type of response which stimulation evoked. By this is meant that stimulation at a particular site under similar conditions could be expected to be followed by a particular kind of behavior, when stimulation at another site would not. Several examples can be given of the bases for stating this.

(*a*) Reports of déjà-vu phenomena occurred only after stimulation at more deeply situated sites of the right needle electrode. It is of interest to note the difference between our findings in this report and those previously reported. Penfield has indicated [9] that such phenomena are to be expected when stimulation is applied in a region of the brain near the focus of abnormal activity. In this patient the clinical electroencephalogram consistently demonstrated abnormality on the side opposite the one in which these stimulation-evoked experiences occurred. (*b*) Verbalizations of feminine sexual strivings followed only upon stimulation of LP5-6 and LN5-6, which, as has been indicated, were at anatomically proximal sites. These same comments apply

to the responses referring to "being alive." (*c*) Reports of mouth sensations occurred at two pairs of sites (LN5-6 and LP5-6, and RN6-7 and RP6-7). The sites in each pair were anatomically close on or near the cortical surface. It is emphasized that the conclusion of the presence of a tendency toward area specificity holds only for the areas which were tested in this study in this patient. Stimulation of other areas, under similar conditions, might have produced similar responses. Comparison with other patients would be necessary before any general conclusions would be warranted. The problems involved in this are mentioned below, but the first prerequisite in such comparison would be placement of the electrodes in similar anatomical structures.

None of the behavioral changes which we have reported bore any consistent or understandable relation to measured changes in poststimulation electrophysiological activity.

The third conclusion refers to the differences in the various responses at different times. There was both an "inter-interview" and "intra-interview" variation in response, even at times to stimulation at the same sites. It is interesting to note the predominant striking findings of the various study periods: In Interview 3 they related to verbal activity and friendliness of verbalization; in Interview 3-a, to déjà-vu phenomena; in Interview 4, to verbalizations of passive compliance and mouth sensations; in Interview 5, to feminine sexual strivings and mouth sensations. Also, even in the same interview, stimulation at a given site did not always bring the same response. This was true not only for such complex behavior as that relating to feminine strivings, but also for the relatively simple direct reports of sensations.

The state of the subject at the time of stimulation seems to influence the ensuing responses. Various factors may cause differences in behavior upon identical stimulations at different times. About some factors, we can do no more than comment on the possibility of their being influential. The time which has elapsed from the original trauma of the operation and untested physiological and chemical factors may be partly responsible, especially for the inter-interview differences.

We attach importance to a consideration of the psychological context in which electrical stimulation occurs. The personality configuration of the subject, including both the current psychodynamic aspects and the psychogenetic aspects, may be an essential determinant of the results of stimulation. For example, we do not conclude that verbalizations by this patient specifically relating to feminine strivings or to passive compliance depended only on an induced physiologic factor upon stimulation. The knowledge about him from the past history and from his behavior in the preoperative interview allowed the inference that a significant pervasive motive in his behavior related to passive-feminine strivings. Our concept is that in this patient, with these ready-present personality factors, stimulation resulted in their more direct expression. Because his responses can be seen as having probably been influenced by past experiences in his personality development, it is also plausible that minute-to-minute changes in his personality functioning and as affected by the vicissitudes of the patient-interviewer relationship could have affected the nature of specific responses. It is this concept which leads to anticipation of difficulty in comparing the findings in one patient with those in another.

We have studied two other patients using essentially the same methods reported here, except that all the data have not yet been as carefully analyzed. In one patient, a man, the electrodes were approximately in the areas to be approached by a bilateral anterior frontal lobotomy. Upon careful observational study of the recorded interviews, no changes whatever could be discerned consequent to stimulation. The second patient was another 11-year-old psychomotor epileptic, in whom the electrode implacements were in roughly the same areas as in

the subject of this report. Although some changes were observed, the manifest behavior was generally quite different from that in the present case. Since placement of the electrodes is manual, no valid comparisons can be begun. However, it is conceivable that stimulation at similar sites in different patients would evoke various manifest responses, depending in part on the personality configuration of the subject.

It is our intent to present mainly descriptive conclusions at present. Yet it seems warranted to speculate briefly about what occurred in this patient when he was stimulated and behavioral change occurred. Our conception is that stimulation at certain points interfered with the balance between drive and defense. For example, after one stimulation he said, without apparent anxiety, "I'd like to be a girl." In the last interview, when he came close to expressing a similar idea under pressure by the interviewer but in the absence of stimulation, he became markedly anxious and defensive. The data do not in themselves resolve the question of exactly how the balance is tipped —whether stimulation only reduced his anxiety or also increased the strength of his feminine strivings or both. The observations just cited, however, do seem to rule out any change that does not include anxiety reduction upon stimulation.

A recent report by Olds and Milner [8] gives evidence that there are parts of the brain in animals, notably in the septal region, where stimulation in itself is rewarding. A like phenomenon in our subject may have been occurring when, e. g., he comfortably reported "feeling good" in conjunction with some of the passive-compliance remarks.

V. Summary

This report deals primarily with the observed behavioral changes consequent to electrical stimulation of various sites within the substance and on the cortex of the frontotemporal region in a boy with psychomotor epilepsy. The implanted-electrode technique was utilized, so that observations were on the awake subject over the course of several days. The method of psychological observation was the interview, continuously recorded, and conducted by an independent observer while stimulations were applied. The psychological data were analyzed clinically and also in such a way as to allow statistical treatment and quantitative statements concerning the behavioral changes without contamination by preconceptions of the effects of stimulation. Stimulation of various areas evoked a range of manifest responses extending from direct sensory experiences (predominantly mouth sensations) to changes in complex behavior patterns. These latter were most uniquely reflected in verbalizations of feminine strivings. There was a tendency toward area differences in the type of responses which stimulation evoked. There was also an observed difference in the types of responses in different interview situations. The possible significance of these observations is briefly discussed. It is suggested that stimulation might alter the balance between drive and defense.

REFERENCES

1. Delgado, J. M. R.: Permanent Implantation of Multilead Electrodes in the Brain, Yale J. Biol. & Med. 24:351-358, 1952.

2. Delgado, J. M. R.; Hamlin, H., and Chapman, W. P.: Technique of Intracranial Electrode Implacement for Recording and Stimulation and Its Possible Therapeutic Value in Psychotic Patients, Confinia neurol. 12:315-319, 1952.

3. Delgado, J. M. R.,; Roberts, W. W., and Miller, N.: Learning Motivated by Electrical Stimulation of the Brain, Am. J. Physiol. 179:587-593, 1954.

4. Delgado, J. M. R.; Rosvold, H. E., and Looney, E.: Evoking Conditioned Fear by Electrical Stimulation of Subcortical Structures in the Monkey Brain, J. Comp. & Physiol. Psychol., to be published.

5. Glaser, G. H.: Panel Discussion: Recent Concepts of Central Neurophysiology: Their Bearing on Psychosomatic Phenomena, Psychosom. Med. 17:337-346, 1955.

6. Kubie, L.: Some Implications for Psychoanalysis of Modern Concepts of the Organization of the Brain, Psychoanalyt. Quart. 22:21-68, 1953.

7. MacLean, P. D., and Delgado, J. M. R.: Electrical and Chemical Stimulations of Fronto-Temporal Portion of Limbic System in the Waking Animal, Electroencephalog. & Clin. Neurophysiol. 5:91-100, 1953.

8. Olds, J., and Milner, P.: Positive Reinforcement Produced by Electrical Stimulation of Septal Area and Other Regions of Rat Brain, J. Comp. & Physiol. Psychol. 47:419-427, 1954.

9. Penfield, W.: Memory Mechanisms, A. M. A. Arch. Neurol. & Psychiat. 67:178-198, 1952.

10. Schreiner, L., and Kling, A.: Behavioral Changes Following Rhinencephalic Injury in Cat, J. Neurophysiol. 16:643-659, 1953.

CORRECTION

In the article "Anxiety and Performance Changes with a Minimal Dose of Epinephrine," by Dr. Harold Basowitz and associates in the July issue of the ARCHIVES, on page 99, left-hand column, the last sentence of the first paragraph should read as follows: "The pure epinephrine powder used in the preparation of this solution contains less than 0.1% arterenol (norepinephrine)."

On page 104, in Table 2, fourth line on the left under Procedure should read: "CFF: Trials (1-5)—(11-15), means."

A Theoretical and Experimental Approach to Problems of Anxiety

ROY R. GRINKER, M.D.
SHELDON J. KORCHIN, Ph.D.
HAROLD BASOWITZ, Ph.D.
DAVID A. HAMBURG, M.D.
MELVIN SABSHIN, M.D.
HAROLD PERSKY, Ph.D.
JACQUES A. CHEVALIER, Ph.D.
and
FRANCIS A. BOARD, M.D., Chicago

I

General laws of psychophysiology have not yet been satisfactorily formulated, despite decades of research by psychologists, psychiatrists, and biologists. In recent years a shift of emphasis toward a psychosomatic approach to problems of human illness has occurred. This has resulted in greater concern with research directly applied to specific illnesses in attempts to pinpoint the role of disturbed emotions in their etiology.

An essential problem in psychosomatic research is the inherent difficulty in determining what factors in the personality and which of its past experiences should properly be correlated with the symptoms of an organ dysfunction. In clinical studies variables are chosen in the psychological and in the somatic systems, and, without clear understanding of their dynamic and temporal relations, they become the basis for the presumed etiological understanding of the psychosomatic disease. Such formulations, attempting to relate two discrete processes, necessarily neglect the mechanisms through which disturbances in one system produce change in the other.

Paralleling such work in psychosomatic research, other investigators have explored the effects of psychological stresses on functions of various parts of the organism. These studies include both experimentally induced stresses and naturally occurring life situations capable of arousing emotional disturbances. A partial survey of the major investigations of this type has been made in previous works.* Sometimes the experimental conditions used were so contrived or trivial as to raise serious questions as to the contributions they could make to our understanding of the more profound, pervasive, and enduring stresses of life. More frequently, single variables for brief periods of time have been the only objects of concern, with little effort to study directly multiple interrelated processes.

In previous work we have utilized soldiers with war neuroses,[10] civilians who were in severe panic or anxiety states,[13] and, most recently, paratroopers in training.[3] In these last studies we hoped that the close observation of men through a period of time in a well-defined situation of danger would allow greater understanding of the mechanisms through which psychological disturbance affects functioning at various biological levels. Although certain advantages of the natural experimental situation are clear, such a study is also limited in the number and kinds of measurements possible, and the inability to assure simultaneity of measurement and to regulate the stress events.

From these various experiences a great

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* References 3, 11, 19.

deal has been learned about the theoretical and methodological problems involved in psychosomatic research. We wish to present in this communication some general statements about these problems, as an introduction to a fairly large series of reports concerning researches of several years past, and still going on.†

In presenting a discussion of our conceptual model of psychosomatic processes within a broad framework, we realize that it is only one of many possible ways of viewing the total organism. Ours has developed from a series of past experiences and pilot studies on anxious subjects, during which we have become aware of the many difficulties inherent in deriving feasible empirical studies from theoretical ideas. No matter how broad or inclusive the initial conceptualization, in practice only segments of biological and psychological functions can be observed, measured, and analyzed. Consequently, in the remainder of this paper we shall present first an over-all theoretical scheme and then the necessarily more limited experimental program derived from it.

II

In part, the present extensive research program was undertaken because we felt there was a need for a methodological model based on tenable theory, applicable to general problems of psychosomatic research. If such a model were fruitful in the study of a single affective state, it might be utilized in studies of other affects and perhaps eventually lead to the formulation of general laws. In the present research we chose to study anxiety because of its great importance in the economy of human existence.

Anxiety has a special role in the adjustive processes of the human organism, both as an indicator of stress and as a precursor of further stress response.[6] We believe that anxiety is a signal to the self and others portending that organismic adjustments are being made to present or expected stress in the dynamically interrelated somatic, psychological, and behavioral processes. At higher levels of anxiety, as in the holocaust of war or unexpected catastrophe, equilibrium becomes so disorganized that adequate behavior, psychological efficiency, and somatic functions are profoundly disturbed. However, milder anxiety is of great significance as a signal of threat to the organism, for it precedes or accompanies active preparation for adjustment and hence may lead to facilitation of functioning at all levels.

Psychologically, the defensive responses may be seen in such maneuvers as counterphobic activity, magical, ritualistic behavior or thought, withdrawal, or character alteration. Thus, anxiety in some past time may be responsible for the development of psychiatric syndromes and personality deformations. Threatening recrudescence in the present, it may intensify the previous defenses or evoke new types of defenses, for free anxiety is one of the most unendurable afflictions of man. As a signal of danger, anxiety is accompanied by a host of interrelated somatic processes which are in the nature of activities preparatory to emergency action. Often these are patterned in individual ways which derive from the subject's early learning. Whatever the later stimulus, the personal pattern is evoked and recognized. With decrease in psychological defenses and lessened control, anxiety mounts and the somatic responses tend to become less discrete and patterned, and more diffuse, global, and undifferentiated. Similarly, the same dedifferentiation of function can be seen in cognitive, conative, and behavioral processes as the defensive utilization of the anxiety signal breaks down.

Free anxiety can be identified as an affect in interpersonal behavior, and as such it is objectively experienced by the subject and communicated by him to an observer. Such anxiety is experienced as an inexplic-

† This is the first of a series of publications and expresses the basic theoretical and methodological problems with which the research program began. It is intended to provide the background for subsequent papers describing detailed techniques and results.

able foreboding of danger or disintegration. As an emotional experience it is necessarily conscious and pressing. We are less concerned here with the condition termed "unconscious anxiety" or with the study of affects which are not reportable. Anxiety can best be defined by the existence of a particular emotional experience. It is relatively meaningless to speak of "unconscious anxiety," intending by that phrase an affect which would be present *if* some defense were weakened or some mode of action prohibited. Unfortunately, much psychosomatic research has been based on assumed affects which were but vaguely implicit in unconscious and underlying processes, expressed only indirectly in symbolic form. Still, as we found in our paratrooper studies, the state in which anxiety is nascent or latent may be related to certain chronic states of somatic activity, and this problem does require study in its own right. What we mean to suggest here is that research in this area requires a clear and consistent definition of anxiety, which should have its referent in emotional experience, rather than being an inferred psychological state from symbolic processes or from physiological concomitants.

In the same paratrooper studies, it was also found that anxiety could be categorized into at least two types—shame and guilt—each with seemingly different correlates in physiological measurements. There seemed to be evidence that these two modalities were associated with at least varying quantities of physiological disturbance, and possibly qualities as well. However, the distinction between types of anxiety is properly made in terms of the parameters of personality discoverable in the subject. We believe it important to define different qualities of anxiety in terms of the time of onset and the life history of the individual, the ego structure, and specific conflict areas. Such research, attempting to describe various qualitative aspects of anxiety, and their possible relations to qualitatively different physiological states, is necessary and important. However, for the subject himself, anxiety is phenomenally unitary, in the sense that he experiences dread and foreboding no matter what its origin or history. Therefore, for our present purposes, we tentatively conceive of anxiety as being a monistic affect and attempt, through the study of personality structure, to tease out such differences as may exist in its qualities.

Before passing to other considerations, it should be noted that free anxiety, having any degree of intensity and duration, is a neurotic phenomenon. However, it is part of a general biological process which, at lower levels, is represented by the apprehension and state of alerting or vigilance, evoked by minor or short-lived dangers, that every human being needs to preserve his life. Anxiety exists when the stress is excessive and the ego controls inadequate.

III

The research workers at this Institute have had considerable experience with various aspects of human anxiety under conditions of severe life stress in combat and less intense life stress in paratrooper training; they have studied patients with chronic states of neurotic anxiety, induced acute emotional responses in anxiety-prone persons and evoked anxiety in healthy persons in contrived laboratory experiments. From these experiences there has been derived a series of general principles and operational concepts which led to the design of our present and ongoing experimental studies.

1. *The Principle of Organization.*—We speak of organization in designating any vital or systematic whole, whether it be a morphological structure, a functional process, or a theoretical concept. Organization is a term usually applied to systems composed of parts or variables which have numerical values. Living systems or conceptual systems are dynamic, since they change through time.[12] Although some systems are composed of arbitrarily selected variables, others consist of variables whose association has been empirically derived.

It is generally accepted that biological and psychological, and perhaps social, systems

are regulated by integrative or homeostatic processes which function to maintain equilibrium within the boundaries of the healthy and adaptive physiological range of organismic functioning.[4] When the integrative determinants or essential variables of a system are strained to a critical point, new or emergency adaptive processes are activated, often with a sacrifice of some functions of the original system. Then, through a "step-function" or a "jump-state,"‡ a new system of organization develops which increases the system's chances of survival or maintenance of organization. Anxiety may be the principal function of a new organized integrated system. If anxiety serves only as a signal, the life of the new system may be temporary and reversibility to the previous organization is a probability. In other situations anxiety may remain chronic—that is, neurotic—and the system remains irreversible. Psychiatrists are well aware of this stability of such an organization, as evidenced by the difficulty encountered in treating patients with chronic anxiety.

As the determinant of a system, anxiety maintains components or processes of organization involving total behavior in the social environment, cognitive and conative functioning, and physiological actions, all of which are adaptive under conditions in which anxiety exists, for as long as it remains. The total system is involved with the environment in that external influences or internal disturbances acting on the anxiety system may augment its component activities or stimulate behavior of the organism to remove itself safely from the dangerous stimulus to which it is highly sensitive, or to attack in attempting to destroy the danger. Thus, even if interest is centered on anxiety as an organization, with its multiplicity of component parts, transactions that involve environmental parameters are ever present.[15] The total social and interpersonal setting in which the observed subject lives and moves should, therefore, be taken into account, either by recording its changes or by controlling its constancy as much as possible.

2. *The Disparity in Time Between the Stimulus and the Total Anxiety Response.*—(*a*) Anxiety Persisting Long After the Application of a Stimulus or After a Cue Has Been "Forgotten": In some earlier experiments we stimulated an area of the human brain above the sphenoid bone in the midline, in the general location of the hypothalamus, through a basal electrode inserted in the nasopharynx.[9] We recorded action potentials from the stimulated area and from the surface of the skull for some time after the cessation of the stimulus. Not only was the basal area excited but large bursts of cortical excitatory waves followed within a few seconds. Then gradually there was a decrement in frequency and amplitude of responses from both the basal and the cortical area. The smooth path of decline was interrupted within a period as long as eight minutes by bursts of excitation in the basal area followed by cortical responses, which finally disappeared, and for a short period the basal area responded spontaneously without cortical activity. Thus the basal area behaved like a condenser. The human subjects suffered intense anxiety at the moment of stimulation and experienced milder bouts of anxiety at the recurrent periods of basal discharge. The corresponding phenomenon in life is a sudden burst of anxiety in response to a crucial situation or a wounding remark with vigorous attempts at recovery of equilibrium by trying to "put it out of mind." Notwithstanding, the person will experience against his will upsurges of anxiety of less intense degree for a long time, often with involuntary conscious recall of the original provoking experience.

(*b*) Behavioral and Physiological Disturbances Persisting After the Affect of Anxiety Has Subsided: During the War we observed profound alterations in behavior, serious physiological changes, and cognitive and conative disturbances in subjects whose anxieties had dwindled to endurable quantities.[10] Long after the stimulus

‡ References 1, 17.

was over, regressive behavior, posture, and speech persisted, suggesting that an initial precipitant could influence the total anxiety process, even though the emotion of anxiety was no longer experienced.

(*c*) Anxiety Appearing Long After the Stimulus Cue: Psychiatrists and psychoanalysts are aware of the fact that real life situations or therapeutic interpretations, even those not consciously recallable to memory, may evoke, after a variable latent period, some or all of the manifestations of anxiety. It may be difficult to determine the crucial stimulus responsible for the anxiety response even in persons under continuous observation because of the time lag between stimulus and response. In the "end-phenomenon" described in the analysis of a paratrooper training program,[3] anxiety often appeared after the stress of training was over.

3. *The Components, Parts, or Subsystems of Anxiety.*—In considering the anxiety process as an organized system composed of subsystems, the essential parts of the process should be identified in order to subject them to rigorous experimental analysis. Empirical data have accumulated to indicate that humans have a wide variety of "personal" responses associated with anxiety. Some report sweating, tachycardia, hyperpnea, diarrhea, "butterfly" sensations, etc., as habitual somatic indicators of anxiety. Others describe purely subjective sensations located "in the head" or "in the mind." Still others indicate disturbances in psychological functions, such as concentration, memory, perception, decision, etc. And some reveal anxiety by behavioral signs of restlessness, manic behavior, or patterns of flight in panic.[2]

The study of anxiety as a process is thus complicated by the wide variety of variables implicated at one time or another as specific or general patterns. Isolation of one or two variables may seem expedient for the sake of simplicity of experimental design, but we believe that the atomistic view of man is misleading and that a larger view, if not entirely molar, is now more productive.[7] Even so, there is a limit to the number of variables that can be studied as components of anxiety because of the limits of endurance of the subject, the interference of systems of measurements, and the available skills. Therefore, it is essential to test in combination those variables, suggested by empirical data to be most significant, that come closest to representing the total range of responses.

Obviously, our choice of variables may be erroneous, even though suggested by experience or logic. These errors could only be determined through the process of testing—which is one of the prime purposes of the research. We need to determine the significance or lack of significance of dependent variables within the anxiety system in order to drop those that are unaltered during change in anxiety and to discover new and more significant ones, located most closely to the central process of anxiety.

4. The *Relationship of Subsystems to the Central Process of Anxiety.*—Our conception of anxiety as an organizing process confronts us with problems of spatial and temporal relations between the "central state" and its peripheral parts. We recognize that anxiety is a function of the central nervous system and that human anxiety by our definition is even more dependent on central nervous functions in that it appears only after the development of consciousness, self-discrimination, concept of future time, and capacity for communication. At the same time, we may view anxiety as a system of psychosomatic organization without reference to any morphological location or limitation to specific organ functions, particularly when the system of anxiety is viewed in transaction with other psychological organizations, in interpersonal transactions, and in group behavior. But when we focus on the internal operations of anxiety, we are in a nexus of psychosomatic functions of organ units and systems. Then organization becomes identical with struc-

ture-function of the central nervous system, the endocrine systems, and their great outflows.

Aside from estimation of degree and kind of anxiety, we became interested in three large subsystems. The first involves the perceptive system, through which cues are received augmenting or decreasing anxiety and which, in turn, is seriously affected functionally in the presence of anxiety. The second involves the reciprocal functions between the hypothalamic-pituitary hormones and their target peripheral glands, such as the adrenal cortex, the thyroid, the gonads, etc. The third involves the direct sympathetic outflow integrated and controlled by the hypothalamus, innervating the visceral organs and the adrenal medulla, thus liberating endocrine substances from various glands and at the nerve synapses and endings.

The combined effect of nervous and endocrine stimulation, in turn, may involve the function of a number of organs, such as the cardiovascular, respiratory, and gastrointestinal systems, and the liver, spleen, adrenal medulla, sweat glands, other smooth muscle, secretory organs, distribution of blood supply, etc. In fact, the activities of these structures are associated in vital metabolism and subject to many local, as well as general, influences. They are less certainly to be construed as essential participants in a stress response the more distantly they are located anatomically or in a functional chain of events. Therefore, we should choose as our significant variables functions as close to the central state as possible. Size of pupil, skin resistance, bowel peristalsis, etc., as symptom indicators common to many types of disturbances, are less important for our theoretical concepts of stress response than pituitary or hypothalamic functions and their immediate neighbors in the sequential chain, which are more important for understanding system mechanisms.

5. *Principles Involving Temporal and Quantitative Relationship Among Subsystems of Anxiety.*—When sequential relationships between parts of the anxiety organization are analyzed, several principles should be taken into account.

(*a*) Resiliency: Biological systems vary in degree of resiliency in individual systems and at various ages. In infants, physiological responses shoot to hypermaximal degrees quickly in response to minor stimuli. In old age, responses are slow, rarely reach the maximum, and decline in intensity gradually. For example, a virus infection may be accompanied by hyperpyrexia in the infant and no fever, or even a subnormal temperature, in the aged. Most estimates of homeostatic resiliency at the biological level have been only partially successful.[5]

In all systems there is a period of inertia, followed by an overaction of function far beyond that of the resting level. Then there is an overreaction in the opposite direction, followed by a period of damped oscillations within successively smaller ranges, until decrement into the basal range is complete. The prototype of this resiliency may be observed during a blood sugar tolerance test.[14] The blood sugar mounts to a high level, until finally insulin effects a reduction of sugar to considerably below the resting level, followed by another rise and then gradually a decline to pre-test levels. Without one's considering exactly which hormones are concerned with the opposite direction of circulating sugar, the elasticity of the system is demonstrable. A variety of enzyme systems is involved.

Many other examples could be given of this ubiquitous biological process. One is the effect of cold on the victim of "sunstroke," with its subsequent hyperpyrexia. The immediate therapeutic response is a rapid fluctuation between varying degrees of hypothermia and hyperthermia, despite the constancy of the body surface temperature.

(*b*) Mechanisms Maintaining Stability Among Subsystems: Within the nervous and enzyme systems stability within physiological ranges is kept constant by processes of reciprocal excitation and inhibition. There is a mechanism to maintain plasma adrenocortical steroids at relatively constant

levels which exemplifies this fact. This is true in spite of considerable apparent variations in the rates of peripheral utilization and metabolism of such compounds. This variation is possible because variations in blood steroid levels themselves influence the amounts of such steroids subsequently released into the blood by cortical tissue. The feed-back operation of this servomechanism functions through the pituitary.[15] The pituitary adrenocorticotropic hormone has been shown to play an important role in the control of the rate-determining reaction for cortical steroid release. While it appears probable that ACTH release is mediated to a large degree through hypothalamic factors, and while it is true that many of the factors controlling ACTH release are not understood, nevertheless circulating corticosteroid levels have been shown to determine the rates of ACTH release.[16] The greater the deviation of blood corticosteroid level from the homeostatic norm, the greater is the associated effect on ACTH release.

(*c*) Hierarchy of Responses: In our paratrooper studies, we found a general pattern of sensitivity in that some reactions would be evoked quickly with minimal degrees of stress and others required maximal quantities of stress. We could distinguish a hierarchy of stress sensitivity among biochemical variables in that eosinophile levels dropped quickly in response to all stress situations.[3] At the other extreme, hippuric acid excretion was extremely stable under stress. Glutathione excretion was intermediate in sensitivity between these two measures. We found another type of hierarchical response indicating that activation of different systems may occur in meaningful sequences. Thus, the blood level of amino acids rose prior to change in hippuric acid. In some subjects anxiety was experienced only after biochemical indices were elevated for some time, and in others the reverse order was held.

An interpretation of the meaning and economics of hierarchy of responses is a priori extremely difficult. At this time we can mention only a few possibilities, since adequate interpretation would depend on future experimental findings. 1. Differences in timing of response may be due to inherent differences in sensitivity or latency of the individual variables within the total anxiety organization, or differences in central thresholds. 2. Some variables, particularly in metabolic processes, may serve as donors for others and may need to build up a significant quantity before another substance can be produced (i. e., aminoacetic acid into hippuric acid). 3. Variables may respond in chain-like fashion, each one tipping over the stability of the next process in a mechanistic sequential chain. 4. Early idiosyncratic conditioning may result in specified responses of certain variables before others that have not been conditioned. 5. Other processes in the complicated homeostatic activities may influence timing of responses, although not of themselves directly involved in an aspect of the anxiety organization which we are observing. For example, epinephrine, liberated through discharge of the hypothalamic-neural mechanism, probably potentiates the peripheral utilization of adrenocortical hormones and also may further activate the production of ACTH.

IV

From the previous discussion of anxiety as an action system possessing a function and an organization, we have indicated some assumptions from which hypotheses may be derived. Since our research is focused on the psychosomatic organization of anxiety, we decided to study the component parts and their relationship to the central state and to each other. As a psychosomatic research, this involves the isolation of specific functions represented by the variables of affect, psychological performance, central nervous system activity, and endocrine secretion.

We propose to measure the activity of a sample of significant variables or subsystems of the anxiety organization as accurately as possible within the limits of

present methods. We hope that each sample can serve as a representative or an index of activity of one of the essential psychosomatic subsystems of anxiety: affect, psychological performance, central nervous system, and hormonal activity. However, since we are investigating the human psychosomatic organization, working with the intact person without harming him, limitations are imposed on our goal of measuring processes as close to the central state as possible. Thus, for our sampling of significant variables we often must be satisfied with indirect indices spatially remote from central functions and often temporarily delayed in appearance. However, for each variable we hope to obtain some notion of its significance, latency, sensitivity to stimuli, resiliency, relationship to other variables, and position on a sequential chain.

We had hoped that we could isolate for each variable a cycle of reciprocal excitation and inhibition, involving a central and a peripheral process. But for this there is required the operation of a negative feed-back, which decreases the activity of an excitatory process. When anxiety is associated with an increase of ACTH, there results an increment in plasma hydrocortisone, which, in turn, decreases the output of ACTH. Thus measurement of hydrocortisone gives some idea of the activity of the hypothalamic-pituitary system. Likewise, intravenous infusions of corticotropin U. S. P. (ACTH) could presumably influence the level of plasma hydrocortisone to different degrees, depending on whether the adrenal gland had been activated by anxiety.

Anxiety may be liberated or augmented by verbally exploring vulnerable conflicts or by temporarily weakening or undercutting psychological defenses. This results in vigorous attempts to reestablish defenses against anxiety or creating new ones, which may be successful in varying degrees.

Perception and decision may be considered as a cycle in that perception of significant cues influences decisions, which, in turn, modify further perception; however, feedback is not automatic but requires information from the environment regarding the accuracy of decisions. Experimentally, the subject can be failed or passed by the observer, but the subject's own level of confidence is no criterion of accuracy or speed of decisions.

Such cycles can be measured by tapping in on them at one pole—measuring anxiety, hydrocortisone, or decision time and accuracy. They may be disturbed by methods applicable to one focus, such as introducing anxiety-producing thoughts, making accurate decisions impossible, or injecting corticotropin, at the same time as anxiety and all other variables are also measured. These measures may give one a good grasp of the significance of variables and their spatial and temporal relationship.

Time relationship is an even more complicated problem, as has been discussed in the preceding section. To ensure measurement of variables in relation to each other, it became necessary to introduce the principle of simultaneous measurements. These are often not possible. Measurements of heart rate, movement, affective state, etc., can be continuous. But psychological performance, circulating hormones, urinary output, etc., can only be measured periodically. We attempted to get as close as possible to simultaneity, at least in a relative sense.

Furthermore, a limited time had to be set for each experiment to obviate the distress of long immobility for the subject. Therefore, in order to observe relationships among subsystems, some of which had a long cycle of activity, long latent period, or slow recovery rate, and others of which were fast-acting, successive blocks of time to span the total spectrum must be utilized. Correlation of values at any of several short periods of sampling time would give quite different results. For this reason it is necessary to conduct experiments observing several variables at different successive blocks of time, moving, as it were, from the earliest phases of responses step by step to the later. If feasible, the experiment itself could extend in several stages, from a short time

to increasing lengths of time, until all systems had recovered completely from the stimulus and had again resumed basal levels.

Our experiments are oriented to give information regarding level, variability, and change as a response to the applied disturbance. They enable us to determine conventional correlations between two or more variables. With successful research into new statistical methods, it is hoped that the pattern of simultaneous response of all variables to a disturbance applied to a single system may be appropriately described.

If patterned groupings could be determined with reference to several types of somatic responses or to anxiety, or if temporal patterns of response of subsystems could be isolated, they would of necessity require correlation with essential personality differences. We assume that significant personality groupings could be found to encompass the content of psychosomatic categories. The important question is how such categories will be defined, especially as to the meaning of the more superficial versus the deeper elements of personality.

For this purpose, each experimental subject from our hospital population is carefully studied psychiatrically. In addition, detailed notes are taken of the patients' spontaneous responses in the experimental interviews and their interactions with the psychiatric interviewer, who discusses the patients' reactions twice in each experimental day. A follow-up interview is conducted after the total experiment is completed. In addition, nurses' notes and the therapist's material are available. Thus, we have extensive psychiatric data from which to view personality in categories or groupings at various levels of abstraction that can be correlated with patterns of anxiety organization either in total or in part.

V

The experimental program undertaken to discover the transactional relationships among several selected aspects of human functioning in the state of anxiety starts with four broad questions: 1. When the level of free anxiety is altered, what concomitant changes occur in each of the other variables? 2. When the existing level of any given variable is influenced experimentally, what concomitant changes, if any, occur in free anxiety? 3. When the existing level of any given variable is influenced experimentally, what concomitant changes, if any, occur in variables other than anxiety? 4. When a change occurs in any variable, such as anxiety, what are the sequences and relative degrees of change in other variables?

In the present studies the functions sampled include affective variables; ego functioning as measured in a perception-decision task, physiological measures, such as cardiac and respiratory rates and percentage time of somatic movements, and biochemical indices of pituitary, thyroid, and adrenocortical endocrine functioning. Each is chosen on the basis of existing knowledge to sample a separate area of functioning believed to be of importance in the total anxiety state. Clearly, many more measures could have been made within each of the areas, and many could have included, as well, areas at present unrepresented.

The nature of the experiment, and the theoretical conception upon which it is based, obviously require the utilization of a number of investigators from several disciplines, each proficient in a variety of special techniques. Not all available disciplines are represented, nor could all of the potentially important variables be measured. The particular variables chosen necessarily reflect the particular knowledge, interests, and backgrounds of the members of the present group.

The Variables Studied

In later reports the rationale, methods of measurement, and findings obtained in each of these areas of evaluation will be presented in greater detail, but, in the interests of an over-all picture, we shall describe them briefly now.

1. *Affective Variables.*—Although in earlier research anxiety was observed and rated as a single affect, in the present studies the approach is broadened to include anger and depression and an over-all estimation of the total emotional response. We do this not only in the interest of completeness but also because anxiety is so often intermingled with other types of emotional responses in the stress situation. By rating all three, observers are forced to discriminate anxiety, anger, and depression and to discover the signs by which each is distinguishable. The emotional ratings are based on a specially devised evaluative interview and on the continuous observation of the subject by observers behind a one-way-vision screen during the entire experimental period.

2. *Perception and Decision.*—A simple task involving the judgment of the relative size of visual forms is used as a measure of the subject's ability to distinguish and judge visual stimuli. Of particular interest is the relationship between the accuracy of such judgments and the time required to make them.

3. *Physiological Measures.*—Heart rate, respiratory rate, and general bodily movements are measured throughout the experiment as indices of disturbance at a physiological level.

4. *Hormonal Measures.*—Plasma hydrocortisone and serum protein-bound iodine are assessed as measures of adrenocortical and thyroid activity. Urinary hydroxycorticoids are also determined as an additional estimate of the status of the adrenal cortex.

Choice of Subjects

We attempt to use subjects with free anxiety, since we are concerned with the changes of functioning in a subject who is already at a relatively high level of disturbance and who, in principle, should show greater changes under stress. However, in ours, as in most clinical settings, it is hard to find patients with any high degree of anxiety which is not quickly subdued by neurotic defenses. Therefore, subjects are chosen who are believed to be most prone to become anxious, a supposition based on the past history of the subject (especially recent) and on the ascertainable weakness of defenses. Even so, it is often found that the experimental intervention stimulates greater defensiveness, often by virtue of implying therapeutic significance to the situation.

All subjects are chosen from a known population in which considerable information is available about the particular personality, major conflict areas, and type of anxiety of each person. Subjects are selected who can be available for the four-day period required by the experiment and who are capable of enduring this degree of restraint. Since our interest is not only in establishing the general patterns of response among the several variables but also in discovering whether there might be types of response patterns, related perhaps to enduring personality characteristics, working with known subjects becomes a principle of central importance. In the design of such research the decision often must be made between the extensive study of a relatively few subjects, in whom individually organized findings can be understood, but who may not give much basis for discovering more general principles, and, on the other hand, the study of large numbers of subjects, each of whom is unknown except for a narrow segment of data which he yields. In the present researches we try to stay between these two poles, studying sufficient subjects to have some conviction of representativeness and, at the same time, knowing each one sufficiently well to have a basis for understanding idiosyncratic patterns.

A further, and important, consideration is that each subject be studied for a sufficient period so that changes in response through time might be seen. Here, again, we stand between two possible experimental designs, the one, in which a larger number of subjects is studied in a particular situation on a single occasion, thus giving little basis for

judging within-subject variability, and the opposite, that of studying a few subjects through extended periods of time, as in the therapy situation, during which considerable within-individual variation can be observed, but of necessity limiting the number of subjects that can be studied and, consequently, knowledge about the variation between subjects. Having the experimental procedure extended in time also allows for the comparison of change within a subject in terms of his own levels of functioning. Using "self-controls" in an area where considerable difference among people is to be expected is, we believe, a necessary procedure.

Experimental Design

In terms of the various theoretical assumptions, a number of pilot experiments were run, in which different variables and conditions of testing were explored. Certain considerations became manifest. The repeated measurement of a number of variables over a period of days limits the choice and frequency of the measures to be used. For example, though one might, in principle, want more points of measurement of a particular biochemical index, the number of blood samples required from a single subject might produce a severe anemia. Interesting variables cannot be used because of interference with other testing procedures. Thus, test methods have to be chosen which can be used within a single experiment on the same subject without interfering one with the other, without requiring excessive time or unusual conditions for administration, and which can be done repeatedly, without earlier testing directly affecting the results of later testing.

The general experimental plan evolved includes four continuous days of testing. The first of these is a preexperimental day, in which the subject is brought to the experimental room and run through each of the procedures. This day is designed to acclimate the subject to the experimental setting and test procedures. The three subsequent experimental days consist of periods before, during and after an experimental intervention (stress stimulus), which differ in each section of the study. Although the measurement of each variable yields different amounts and types of information—heart and respiratory rates are recorded continuously throughout each of the days, while the evaluation of perceptual functioning depends on a test given once in the "before" and once in the "after" period—each of the major periods of the experimental day is viewed as a single unit within which all measures are conceptually "simultaneous." The value of each variable for the entire period, whether based on the mean of a number of measures or on a single measure, is taken to represent the level of functioning in that system for that period.

A central event on each of the experimental days is a stress stimulus condition which is intended to induce change in some aspect of the total system. This event, describing the "during" period, separates the measures made before and after on each of the three experimental days. Thus, it is possible to compare the amount of change in each variable separately and jointly as a function of the inducing stimulus. The effort is made to increase the intensity of the experimental stress on each of the three experimental days in the hope that different threshold responses for the several variables can be exposed.

In the over-all plan the experiment is to be divided into four studies, each involving a different stress stimulus designed to affect the functioning of each of the systems in turn. Different groups of subjects, matched in their anxiety proneness, are to be used for each of the conditions. These involve (1) increasing anxiety itself by use of a stress interview designed to confront the subject with unconscious or unacceptable material and to challenge certain defenses; (2) affecting perception and decision making by a procedure impugning the accuracy of the subject's perception, and (3) disturbing the adrenocortical system

through the intravenous injection of corticotropin. In each of these different experiments the same basic design is used and the same measures of affect and other functioning are made before and after the experimental intervention. Clearly, each of these stimulus situations differs; some, like corticotropin, can be regulated for the entire duration of the experimental day, while others, like the stress interview, may often have short-lived, or even quite unpredictable, consequences. Still, we are hopeful that using the same basic evaluative design—three days of pre- and postmeasurement in a number of selected variables—and changing the inducing force so that its point of application represents, in turn, each of the different systems may provide an approach to the questions raised earlier and a model for experimentation in the psychosomatic field.

REFERENCES

1. Ashby, W. R.: Design for a Brain, New York, John Wiley & Sons, Inc., 1952.

2. Basowitz, H.; Korchin, S. J.; Oken, D.; Goldstein, M. S., and Gussack, H.: Anxiety and Performance Changes with a Minimal Dose of Epinephrine, A. M. A. Arch. Neurol. & Psychiat. 76:98, 1956.

3. Basowitz, H.; Persky, H.; Korchin, S. J., and Grinker, R. R.: Anxiety and Stress, New York, The Blakiston Company (division of McGraw-Hill Book Company, Inc.), 1955.

4. Cannon, W.: The Wisdom of the Body, New York, W. W. Norton & Company, Inc., 1939.

5. Freeman, G. L.: The Energetics of Human Behavior, Ithaca, N. Y., Cornell University Press, 1948.

6. Freud, S.: The Problem of Anxiety, New York, W. W. Norton & Company, Inc., 1956.

7. Grinker, R. R.: Psychosomatic Research, New York, W. W. Norton & Company, Inc., 1953.

8. Grinker, R. R., Editor: Toward a Unified Theory of Human Behavior, New York, Basic Books, Inc., Publishers, 1956.

9. Grinker, R. R., and Serota, H. M.: Studies on Corticohypothalamic Relations in the Cat and Man, J. Neurophysiol. 1:579, 1938.

10. Grinker, R. R., and Spiegel, J. P.: Men Under Stress, Philadelphia, The Blakiston Company, 1945.

11. Hanfmann, E.: Psychological Approaches to the Study of Anxiety, in Anxiety, P. H. Hoch and J. Zubin, Editors, New York, Grune & Stratton, Inc., 1950.

12. Lillie, R. S.: General Biology and Philosophy of Organism, Chicago, University of Chicago Press, 1945.

13. Persky, H.; Grinker, R. R., and Gamm, S.: Correlation Between Fluctuation of Free Anxiety and Quantity of Hippuric Acid Excretion, Psychosom. Med. 14:1, 1952.

14. Soskin, R., and Levine, R.: Carbohydrate Metabolism, Chicago, University of Chicago Press, 1952.

15. Spiegel, J. P.: A Model for Relationships Among Systems, in Toward a Unified Theory of Human Behavior, R. R. Grinker, Editor, New York, Basic Books, Inc., Publishers, 1956.

16. Sydnor, K. L., and Sayers, G.: Blood and Pituitary ACTH in Intact Adrenalectomized Rats After Stress, Endocrinology 55:621, 1954.

17. Toman, J. E. P.: Stability *vs.* Adaptation, in Toward a Unified Theory of Human Behavior, Roy R. Grinker, Editor, New York, Basic Books, Inc., Publishers, 1956.

18. Wiener, N.: Cybernetics, New York, John Wiley & Sons, Inc., 1948.

19. Wolff, H. G.; Wolf, S. G., and Hare, C. C., Editors: Life Stress and Bodily Disease, Vol. XXIX, Proceedings of Association for Research in Nervous and Mental Diseases, (1950), Baltimore, Williams & Wilkins Company, 1950.

Malingering: "Diagnosis" or Social Condemnation?

Analysis of the Meaning of "Diagnosis" in the Light of Some Interrelations of Social Structure, Value Judgment, and the Physician's Role

THOMAS S. SZASZ, M.D., Syracuse, N. Y.

According to Webster, malingering is the "feigning of illness or inability in order to avoid doing one's duty." It is consistent with this definition that in our actual daily life malingering is rarely an issue, except in the social framework of the military service. In civilian life, nowadays, the question of malingering is sometimes raised in cases involving litigations with insurance companies over alleged damages to the patient's health and in connection with criminal offenders who may plead "insanity." Accordingly, this (alleged) syndrome is discussed usually as a part of military psychiatry.* The concept of "malingering," however, has theoretical implications and significance which far transcend this framework.

Clarification of the problem of malingering is of interest for the following reasons: First, we touch here on a subject which has a clear and immediate relevance to the wide area of medicolegal matters. The relationship between psychiatry and law is currently a much-discussed subject. Analysis of our notions concerning "malingering" cannot fail to shed further light on this topic.

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Professor of Psychiatry, State University of New York, College of Medicine, Syracuse 10, N. Y.

* No attempt is made in this paper to present a review of the extensive psychiatric literature on the problem of "malingering." The reader's attention is called to Eissler's essay,[6] which contains numerous references to the literature.

* Second, inquiry into the nature and meaning of "malingering" makes it necessary to examine what we mean by the term "diagnosis." "Malingering" is often used as if it were a "diagnosis," much as is hysteria or schizophrenia. This is a grave error, and I shall try to show why and how malingering differs from our usual conception of a psychiatric diagnosis.

Finally, the problem of "malingering" provides an opening wedge into the large and currently also much-discussed problem of antisocial behavior. Indeed, no examination of "malingering" seems possible without touching on certain aspects of the sociopsychology of antisocial action ("psychopathy," delinquency, criminality).

The purpose and method of this essay differ from those customarily encountered in studies of malingering. The latter usually take this label as a genuine diagnostic category and proceed to describe its (alleged) psychological characteristics. Instead of this approach, I propose to view "malingering" from a broader perspective. I shall question its meaning as "diagnosis," call attention to its legal and sociological implications, and, in general, try to examine and analyze the very concept of "malingering" from a point of view combining psychiatric, sociologic, and philosophic considerations.

Is Malingering a Diagnosis?

All psychiatric and psychoanalytic authors who use this term speak of "malingering" as if it were a diagnosis, on equal footing with concepts such as conversion hysteria,

compulsion neurosis, or schizophrenia.† In my opinion, this is a logically unsupportable position, for it ignores (or denies) what is probably the most important element in the meaning of this word, namely, that it is applied to a bit of behavior which society, and presumably the psychiatrist himself, regards as morally despicable. In order to discuss the question "Is malingering a diagnosis?" we cannot help also asking, "What is a diagnosis?" The posing and answering of these questions is by no means an exercise in pedantry. Diagnosis, Webster reminds us, is "the art or act of recognizing disease from its symptoms; also the decision reached." We might add that it has two important aims, one being to help the physician himself in selecting the proper treatment for the patient "afflicted" (so to speak, with the "diagnosis") and the second, to enable him to communicate with his fellow workers.

The communicative meaning of a diagnosis is, obviously, of great importance in connection with "malingering." Insofar as a diagnosis functions as a communication concept, it is clearly designed for the physician to communicate with his colleagues. We are familiar with the semantic and psychological complications which arise when diagnoses are communicated to patients, or their families, who do not "understand" them in the same way as they were intended.[8]

† It must be noted, in this connection, that the problem of what constitutes a "psychiatric diagnosis" is itself an exceedingly complicated matter, fraught with many difficulties from the point of view of scientific clarity and usefulness. For the sake of simplifying matters, in this essay we shall regard the conception of a "psychiatric diagnosis" as something definable and useful and shall focus on the sociopsychological meaning of this notion. It is important to remember throughout such a discussion that the overbearing motive behind this concept is a philosophical position (whether explicitly recognized or not) which insists on forcing social behavior into the framework of medicine, and thus views some modes of action as "healthy" and others as "diseased."[28]

In military life, the implications of the communicative aspect or meaning of a diagnosis are far reaching. Any given diagnosis has, at the very least, the following three functions in this situation: 1. It represents the physician's (psychiatrist's) concept of what is "wrong" with the patient (e. g., fractured leg, acute appendicitis, schizophrenia). 2. It serves as a method of communication between him and other physicians. That is, each "diagnosis" calls for appropriate "treatment" (e. g., acute appendicitis is a command to the surgeon to operate, etc.). 3. It represents a method of communication between the physician (psychiatrist) and the military authorities who are the patient's superiors. Actually, similar considerations pertain also to civilian life, except that if the patient is an adult, the diagnosis is usually a private matter between him, his physician, and perhaps other physicians, and does not (or should not) involve the patient's social and professional organization.

For the present, we shall not be concerned with the first two meanings of a diagnosis (i. e., for the physician himself and as an intraprofessional concept) and shall concentrate on its third meaning (i. e., communication between the physician and the patient's social or professional organization). If a diagnosis is going to be used in this way, it must fulfill, it seems to me, at least two important criteria. 1. The recipient of the message must receive from the "diagnosis" something closely approximating what was intended by the physician. 2. The diagnosis must carry a minimum of moral overtones; it must essentially be a clear description and explanation of behavior, not its praise or condemnation.[3] Now, as regards the first criterion, unambiguity of the communication, this is unsatisfactory, whether it is between psychiatrist and military authorities, or between psychiatrist and his civilian medical colleagues.[4] Since this is equally true, however, for all psychiatric diagnoses, it presents no distinct problem for any one

syndrome. Clearly, it is the moral condemnation implicit in the term "malingering" that is of the greatest relevance in this discussion. While this is obvious enough, it appears that its implications must be persistently overlooked or ignored, for otherwise this word would long ago have been dropped from the psychiatric "diagnostic" vocabulary (as have concepts like "demoniacal possession" or "falling sickness," which have now only historical significance).

A simple illustration will show that malingering cannot be rationally regarded as a "diagnosis" in the military, or any other, setting. The categories of paranoid and catatonic schizophrenia are two good descriptive labels. Whether or not they are "correctly understood" by the nonmedical authorities, it is of no advantage or disadvantage for a person to be labeled with one of these diagnoses in preference to the other. Moreover, no moral connotations are attached to them (except that the patient may be "rewarded" for both by the payment of a disability compensation). In contrast to this, to the military authorities malingering means a bit of criminal behavior. This "diagnosis" is, in fact, nothing less than a covert command from the physician to the military judicial authorities to punish the patient.[25] The traditional "differential diagnosis" of malingering and hysteria is nonsense if it disregards this important fact. It seems to me that while the concepts of primary and secondary gain have much merit in this connection they retain a moralistic (and misleading) flavor, according to which primary gain is unconscious and beyond "willing," whereas secondary gain is conscious and therefore "willful." All facts considered, it appears necessary to conclude that malingering is so heavily impregnated with the moral condemnation of the behavior to which it is applied that its usefulness as a scientific, diagnostic term is completely vitiated.‡

‡ We touch here on the nature and use of symbols. Langer's following comments explain further why "malingering" is such a "distracting" symbol. "Another recommendation for words is that they have no value except as symbols (or signs); in themselves they are completely trivial. This is a greater advantage than philosophers of language generally realize. A symbol which interests us *also* as an object is distracting. It does not convey its meaning without obstruction. For instance, if the word "plenty" were replaced by a succulent, ripe, real peach, few people could attend entirely to the mere concept of *quite enough* when confronted with such a symbol. The more barren and indifferent the symbol, the greater is its semantic power"[10] (page 61).

"Malingering" from the Viewpoint of Life as a Game

When a person calls another a "malinger," what does he tell us about himself? He tells us that the "malingerer" is, so to speak, "getting away with something." It is implicit in this judgment that the observer, as well those whom he is addressing, consider (even if not consciously) the duties which the malingerer is thought to shrink as oppressive, unpleasant, or dangerous, in brief, such that they, too, would like to free themselves from these duties. This social validation of the duty as something undesirable and oppressive, even though it may have many gratifying facets, too, is clearly illustrated by the example of compulsory military service. The slang term "goldbricking," which means malingering, would not be generally understood if it were not assumed that the *wish to not be in the service* was not shared by everyone. It seems useful, therefore, to suspend our psychiatric tendency to view malingering in terms of "psychopathology" and psychical "mechanisms," and, instead, to look upon it from the viewpoint of life as a game. Malingering, then, is the same as *cheating*. The "game" in which the malingerer cheats (in this frame of reference) is, moreover, not a playful interlude in life, but is a segment of life itself. Its rules are defined by society—as laws, which are explicit, and as more subtle social conventions, which are usually implicit in the culture and are not formally stated. Certainly, the assertion that malingering in wartime is regarded as a

form of "cheating" does not require documentation. Eissler has emphasized that "malingering nearly always shows us the individual in direct rebellion against society."§ It must not be thought, however, that this constitutes a distinctive feature of "malingering," since we know that so-called criminal behavior, as well as illnesses of all types, may be so motivated, or, in any case, may be looked upon from this point of view. For example, not long ago all sorts of behavior now regarded as "psychiatric illness" was thought of as "malingering." Even today, those unsympathetic to the psychiatric mode of thought concerning human behavior tend to think (and speak) of deviant behavior as "malingering."

The point which I want to make is simply this: Insofar as we look upon life as a game—its rules consisting of modes of behavior prescribed by society—all behavior which violates the rules may be regarded as "malingering." Thus, the hysteric in Charcot's day was regarded as evading the "duties" of procreation and other adult female "responsibilities"—and was therefore thought of as a malingerer—a view by no means altogether obliterated by psychoanalytic discoveries. It is important to note that in this view the "rules of the game" are held inviolate and unchanging. Those who violate them incur the observer's moral opprobrium.[18] Freud's contribution, among others, was to focus attention on the "rules of the game" (civilization, the family situation, etc.) and thus to reveal the determinate and meaningful character of all modes of adaptation to these rules. He thus lifted "neurotic" behavior from the realm of morals into that of science. From the point of view of science, however, the social structure—whatever it might be—cannot be regarded either as fixed or as "good." From this line of thought, too, we arrive at the conclusion that "malingering" cannot be used in a scientific sense, since it embodies an unquestioning acceptance and approval on the part of the observer of the rules which are prevalent in society at any given time.

An example will perhaps clarify the foregoing assertion. During the last war, approximately 10,000,000 Americans were drafted for service in the armed forces. The laws and regulations governing life in general, and acceptability in the military service in particular, were clearly set forth and were well known by the public. There were, among these regulations, certain standards regarding physical and "mental" health to which one had to measure up to be acceptable for service. The reasons for these standards of health had, on the whole, little or nothing to do with practical matters ("utility") and were governed, rather, by unconscious moral considerations. There is little in most military duties that requires a man to be any healthier than he would have to be to earn a living as a civilian. It is, rather, one of the social conventions of Western civilization that a man must be healthy before he can be conscripted for military service. There is a strong analogy here with the treatment accorded to "criminals" who are aged or ill; that is to say, they are treated more leniently than they would be if they were young and healthy. As I have suggested elsewhere,‖ the most probable explanation for this seems to lie in the assumption that assurance about the soldier's or individual's health serves to mitigate the guilt which society—and its representatives (judge, jury, draft board, etc.)—tends to feel when it damages (sentences) a criminal, or when it exposes a soldier to possible injury or death. Thus, matters of health constitute, in part, the rules of the game, which could be paraphrased as follows: "You must be healthy in order to be drafted and possibly be killed; if you are sick, you are excused from such onerous duties—indeed, you might even get financial compensation for your suffering." Considerations of the sociopsychology of so-called "service-incurred" disabilities would carry us too far afield. Suffice it to note, in this

§ Eissler,[8] p. 218.

‖ References 25 and 26.

connection, that this entire problem, too, appears to me best understood when viewed as an attempt on the part of society to expiate its own feelings of guilt and responsibility in connection with the injured soldier's fate. It is not governed—and makes little sense when so viewed—by what "actually" happened to the alleged victim.

Let us return to the theme of the criteria of health as a part of the social rules governing military service.[24] This notion is of the greatest importance for our subject—malingering—chiefly for two reasons. First, it shows us that the rules themselves contain many proper, socially condoned "moves" (or ways of playing the game without cheating), which make it possible to evade an onerous duty. Second, it provides the essential clue for our understanding of the psychiatrist's role in this social structure.[6]

It is clear from the premise that one must be healthy in order to be acceptable for military service, that a premium is put upon illness for those who want to avoid such service. By being ill one can avoid being drafted and still play the game entirely according to the rules. Neglect of this facet of the problem, it seems to me, has led Eissler to pose the following problem:

> Reluctance to serve in the armed forces has been so general that the problem could be seen rather in the fact of millions not having malingered than in the few who did. Yet such an approach would lead us to overlook the specific combination of personality factors which make malingering possible.¶

The fact is that millions upon millions were rejected because of physical or psychiatric "disability," and further millions avoided military duty by the appropriate selection of occupations. If "malingering" is a matter of motives, all these modes of behavior would qualify for this disparaging term. The traditional use of malingering, however, is more truly operational than are many concepts of motivational psychology. Accordingly, malingering is reserved for those modes of conduct which aim—and perhaps achieve—avoidance of an unpleasant duty by some mode of behavior *expressly disallowed by society.*# What are such modes of behavior in our present culture? The answer to this question brings us face to face with all of our philosophical preconceptions and prejudices about health and illness. Briefly, we can state that aches and pains not clearly attributable to somatic lesions are among the most disreputable "symptoms" which one can have today. This is particularly true in the military services. Accordingly, every soldier who complains of headache is suspected of "malingering" (in the sense of wanting to get out of an unpleasant situation). On the contrary, should such a headache lead to the diagnosis of brain tumor, he will be retired from the service and will receive financial compensation for it for the rest of his life.

It follows from the consideration that matters of health constitute in part the "rules of the game" of military service that the physician's role in this social structure is significantly different from his role in the private practice of medicine.* In the latter, his main concern is his patient, who—metaphorically speaking—hires the doctor to repair his damaged body. In the military situation, the physician is not "hired" by the patient at all. In the induction station, for example, his role is to determine who is acceptable for service according to the criteria set forth. Similarly, in a military hospital or at the front lines, the physician is primarily an agent of the military service. Whatever his relationship to the body (or mind) of the soldier, he retains the important function of determining the patient's role vis-à-vis the military organization (e. g., evacuation from danger at the front,

¶ Eissler,* p. 218.

Thus "fraudulent enlistment" is not thought of as "malingering," since it constitutes a mode of escape from unpleasant duties (at the "home front"), which is expressly allowed by the morality of our society. (For further remarks concerning the difference between "malingering" and "fraudulent enlistment," see the last section of this article.)

* References 20 and 21.

retention in or discharge from the service, etc.).

A confusion or clashing of the aforementioned two roles constitutes one of the most important sources of trouble in military medicine, and particularly in military psychiatry. Thus, civilian physicians drafted into the service have a tendency to identify with the patient in the latter's conflicts with the military authorities. They are then regarded as "poor officers." On the other hand, the career medical officer is expected to have his primary allegiance to the military organization. In all those situations, then, in which the needs of the individual and of the service cannot be harmonized, the physician is caught in a serious dilemma. This problem is, obviously, commonest in psychiatry, much less of a problem in surgery, and no problem at all in pediatrics. The pediatrician in military service never encounters a situation in which his patient's needs do not coincide with the needs of the service. The psychiatrist encounters many such cases. It is sheer hypocrisy to maintain that one can take an impartial position in the face of such conflicting needs and be able to do "justice" to both sets of obligations.†

In summary, then, from the point of view which we are now considering, it would seem that the physician's (and psychiatrist's) chief function is that of an umpire: He is an agent or representative of the social body (the game), and it is his duty to make sure that everyone plays the game according to the rules. Like the umpire in a tennis or football game, his duty is to watch, apprehend, judge, and sentence those who "cheat" or otherwise violate the rules. It is clear, moreover, that he can do this job best by identifying psychologically both with those who set the rules and with the players. He must be "at one" with the rules —with the social structure, whatever it might be and however it might change—for what good would it do him, in the performance of his job, to question the rationality of the rules themselves? Such an attitude would obviously tend to interfere with his performance as "umpire." He must, however, also be identified with the players and must be familiar with the game as an active performer, or else he would be easily fooled by the "tricks of the game." Just as the umpire assumes that every player is out to win—by fair means or foul—so the military physician (insofar as he plays this particular role) assumes that everyone is ready to use illness for illegitimate purposes. If such assumptions were, indeed, not dominant features of competitive sports, why should there be umpires? Similarly, the universal premise in our culture that

† An entirely similar clashing of roles occurs in present-day psychoanalytic training: The training analyst occupies the dual position of therapist vis-à-vis the candidate-patient and authorized teacher vis-à-vis the institute or analytic society. Both roles clearly define his "responsibility." According to the former, it is to the candidate; according to the latter, it is to the professional group, of which the training analyst is a representative ("responsibility" is often further projected out into society, so that teachers generally feel that they are the representatives, or even the defenders, of the best interests of "society" in general, or of potential patients in particular, in the case of medicine and psychoanalysis). The conjoint form of the expressions "training-analyst" and "medical officer" is itself a statement of the double role described above. While all this is common knowledge, there remains a persistent belief in such situations of "double responsibility" that with sufficient skill and honesty it is possible to reconcile the two roles and to satisfy the needs of all the parties involved. I want merely to call attention to what appears to be a complex matter which requires careful attention and which does not permit of easy generalizations. It seems to me, further, that in psychoanalytic training, just as in military medicine, the training-analyst (physician) can function effectively only if there is no conflict between the needs of the candidate (soldier), on the one hand, and the needs (or what the analyst *thinks* are the needs) of the analytic community (military service), on the other hand. Should the needs of these two "systems" be, or appear to be, in conflict, the training-analyst's role readily becomes restructured, so that he becomes a "mediator" between two clashing systems with (apparently) mutually exclusive aspirations. In this role, his usefulness for either therapy or teaching is obviously vitiated.

everyone is a potential malingerer accounts for the role of the physician as an expert arbiter who must decide whether a person is "ill" within or outside the rules which society sets for illness. Often enough physicians refuse to play this role and seek instead to alter the "rules of the game," that is, the standards by which society judges one mode of conduct as "illness," and therefore legitimate, and another as "criminality," and therefore reprehensible. We shall consider this phase of our subject in the following section.

"Malingering" from the Viewpoint of Psychopathology

Psychiatrists often are, or seem to be, committed to a point of view according to which they try to interpret all sorts of behavior in terms of "psychological illness" or "maladaptation," in brief, as psychopathology. This era was probably ushered in by Freud's study of Leonardo da Vinci [11] and led to numerous interesting psychoanalytic "pathographies" of famous people. Such studies contributed richly to our understanding of human behavior, including the psychology of artistic and scientific creativity.

It is one thing, however, to use a fruitful point of view, such as was opened up by psychoanalysis, as a frame of reference from which to examine all sorts of phenomena (such as art, religion, and education), and it is quite another to put forward the viewpoint itself as the *answer* to perplexing problems. Psychiatrists, particularly psychoanalysts, have at times done just this. Three areas of human living come to mind as illustrating this trend most clearly: criminality, the problem of malingering, and some aspects of political leadership. (These are, however, by no means the only ones.) It is common for psychiatrists to maintain that "crime" is an "illness" and that the "criminal" is an "ill person." Balint, for example, stated clearly and simply, "Being a doctor, I propose to treat criminality as an illness." ‡ This view not only is common today among psychiatrists, but is also considered to be "progressive," and especially meritorious on account of its alleged "humaneness."[26]

The problem of malingering is, in this respect, similar to that of criminality. Instead of asking exactly what is meant by this term—or instead of defining and scrutinizing the concept itself—psychiatrists have accepted "malingering" as an entity, much like pneumonia, and have proceeded to describe its characteristic "psychopathological" features. To proceed in this way amounts to a confusion of our mode of operation (i. e., our method of observation and communication) with which we approach a problem with the "explanation" of the problem itself. For a psychiatrist to maintain that he will approach the problem of crime as an illness is not very different than for a neurophysiologist to proclaim that he will approach the problem of neurosis in terms of cybernetics. Such statements are declarations of faith and explicit affirmations of one's mode of approach to a problem. If the method in question possesses much prestige, the very act of adherence to it may appear as a meritorious accomplishment. This is, however, sheer illusion. Thus, to maintain that criminality, malingering, or some aspects of political leadership are matters of "psychopathology" is to indulge ourselves in such an illusion. By so doing, we merely substitute the vague and all-inclusive notion of "mental illness" for all sorts of other problems.

Let us turn our attention now to a consideration of the specific pitfalls which entrap the psychiatrist who approaches malingering as if it were a "syndrome" which "exists in nature." What does he

‡ Balint,[1] p. 262.

find? He finds that in which he is most interested.§ Thus, Eissler, who has contributed much to our understanding of ego-psychology and schizophrenia, arrives at a conception of "malingering" in line with these interests. His conclusion, at the end of his long and scholarly psychiatric essay on malingering, is as follows:

It can be rightly claimed that malingering is always the sign of a disease often more severe than a neurotic disorder because it concerns an arrest of development at an early phase. Moreover, whereas in neurotic disorders the pathological process is limited and the functional capacity of the rest of the personality is at least potentially preserved, malingering is a symptom of a disorder which does not leave any single structure of the personality unaffected. It deserves special clinical interest because it is a disorder which is in between alloplastic and autoplastic disorders, and thus maintains an unique position in clinical classification. It is the result of a rigidity of the ego, of its loss of capacity to respond organically to stimuli. It is a disease which to diagnose requires particularly keen diagnostic acumen. The diagnosis should never be made but by the psychiatrist. It is a great mistake to make a patient suffering from the disease liable to prosecution, at least if he falls within the type of personality I have described here.‖

Wertham's views¶ stand in interesting contrast to those of Eissler. He considers "malingering" in connection with criminality, specifically murder, a subject which is of special interest to him. Wertham's opinion is that some murderers are "sick," suffering from a syndrome which he carefully describes and calls the "catathymic crisis." Others, in contrast, commit murder and simply "malinger" insanity. He assumes without question that it is for the psychiatrist to make the distinction as to which murderer is "sick" and which is "not sick" and thus, in essence, to determine their subsequent fate. The following are excerpts from his writings relevant to our thesis:

The topic of simulation, of the malingering or faking of mental disease, is unpopular in psychiatric circles. Not a single really good monograph exists on the subject. Beating the law through simulation of a mental disease is not merely a psychological phenomenon, it is also a social one. Crime does not pay, but criminals sometimes do #. . . . I have done research on the simulation of mental disease for a long time and found out a number of curious things. There is a strange, entirely unfounded, superstition even among psychiatrists that if a man simulates insanity there must be something mentally wrong with him in the first place. As if a sane man would not grasp at any straw if his life were endangered by the electric chair.*

In his book, "The Show of Violence,"[28] Wertham presents the story of several murders and murderers. Some murderers, as mentioned, he considers to have suffered from a "catathymic crisis," and are labeled "sick." Two of the men who committed murders, however, he states were "malingerers" (Martin Lavin and Forlino).

The case of Forlino is of particular interest in this connection. This man killed his 3-month-old nephew with a hunting knife. Prior to this, he had been arrested for exhibitionism; he was also overtly homosexual. Still, Wertham writes:

It was only too clear from his account that he had definitely and consciously been simulating a mental disease at the time he was in the psychiatric hospital. He had played crazy. But why? Long experience has convinced me that when criminals simulate insanity the charge against them is usually serious†. . . . However enthusiastic you may be about the use of psychiatry in jurisprudence, there should be little doubt that the Forlino case belongs to jurisprudence and not to psy-

§ "There is the problem of the psychology of the person who makes the diagnosis of malingering"[9] (page 224). With these words Eissler cautioned against this danger, but did not pursue its implications. The fact that malingering as a psychiatric "syndrome" is undefined makes it particularly suitable for each psychiatrist to find that sort of psychopathology characteristic of it in which he is most interested. This, I believe, accounts for the fact that the foremost men in our field have made quite diverse comments about this alleged syndrome; and each of these notions is reasonable and more or less valid for the material at hand.

‖ Eissler,[9] pp. 252-253.

¶ References 27 and 28.

Wertham,[28] p. 48.

* Wertham,[28] p. 49.

† Wertham,[28] p. 193.

chiatry.‡ The whole story is an unending game of hide-and-seek between an individual and the authorities §. . . . Despite his glimmering of guilt feelings, Forlino is a personality of unheard-of moral callousness. No clinical psychiatry, no psychoanalysis, no biology can yet tell us the cause and cure for such a person. But the victims need protection.‖

Quite aside from whether one agrees or not with Wertham's ideas about the "catathymic crisis," it seems clear that his conclusions concerning the Forlino case illustrate the personally arbitrary nature of what is considered to constitute a "mental disease." Forlino, who was arrested for exhibitionism, is "not sick." This implicit assertion of Wertham's and his plea that this case "belongs to jurisprudence" does not mean anything other than that he wishes the offender to be punished. Others, whom he does not consider to be "malingerers," should not be "punished," but should be "treated." However reasonable this may sound, it must be kept in mind that the psychiatrist, were he to function in this manner, would play two distinct and separate roles: first, the role of a scientist, an expert in the study of human behavior and, second, the role of an arbiter, a holder of social power, who decides which modes of behavior shall be punished and which rewarded.

The following excerpts are quoted to show further opinions about malingering. Here is what Glover says:

In the majority of cases, particularly when a cluster of phobias is maintained, anxiety hysterics extract a considerable unconscious advantage from their symptoms. They usually dominate the household of which they are a member and can marshal their various phobias to meet every awkward emotional contingency. So marked is the factor of secondary gain that it has been regarded by some observers as an etiological factor. But this is to confuse hysteria with simulation and malingering. The continual exploitation of secondary gain is, however, a good diagnostic pointer.¶

For Menninger some forms of "malingering," at least, constitute examples of "focal suicide." He wrote:

To the extent that a neurotic person consciously makes use of the secondary gains of his illness, he is of course a malingerer, and to just the extent that he is conscious of this does the neurotic patient deserve to share in the opprobrium that attaches to malingering #. . . . Malingering of the self-mutilative type may thus be described as a form of localized self-destruction which serves simultaneously as an externally directed aggression of deceit, robbery and false appeal. The aggression is of such an inflammatory sort that it, in turn, obtains for the malingerer not only sympathy, attention, and monetary gain (at first), but, ultimately, exposure, reproach and "punishment."*

Bleuler stated the opinion:

Those who simulate insanity with some cleverness are nearly all psychopaths and some are actually insane. Demonstration of simulation, therefore, does not at all prove that the patient is mentally sound and responsible for his actions.†

Henderson and Gillespie consider "simulation" in the differential diagnosis of "psychoneurotic reaction-types" and contrast it specifically with hysteria:

The dividing line between hysteria and simulation is often very difficult to draw. Simulation is the voluntary production of symptoms by an individual who has full knowledge of their voluntary origin. In hysteria there is no such knowledge, and the production of symptoms is the result of processes that are not fully conscious.‡

Noyes's view of malingering § is the same as that of Henderson and Gillespie.

‡ Consider, in the way of contrast, the following statement by Max Radin (an eminent attorney and professor of law at the University of California): "The law, I have said, makes the humiliating discovery that it really has no subject matter of its own. Throughout the nineteenth century, men who busied themselves with the science of law, chiefly in Germany, thought they could isolate acts and facts which were characteristically legal. They called them "juristic" acts or facts or else "acts or facts in-the-law." There really are no such things. Any act or fact can be juristic, no matter what it is, if it becomes necessary for some legal institution, a court or an administrative agency, to deal with it"[22] (page 78).

§ Wertham,[20] p. 208.

‖ Wertham,[20] p. 210.

¶ Glover,[12] p. 157.

Menninger,[18] p. 286.

* Menninger,[18] pp. 295-296.

† Bleuler,[5] p. 191.

‡ Henderson and Gillespie[18] p. 196.

§ Noyes,[19] p. 284.

Reference to other authors shows still further divergences of opinion concerning the nature of "malingering." ||

The foregoing quotations demonstrate the following two significant phenomena: 1. Psychiatrists regard "malingering" as a clearly identifiable "clinical syndrome." 2. Many wholly dissimilar views—some diametrically opposed to others—are set forth as descriptions and psychiatric theories of "malingering." This state of affairs illustrates the epistemological confusion about the problem of "malingering," mentioned earlier. No amount of clinical psychiatric investigation alone will clarify this muddle.

It must not be thought, however, that the foregoing psychiatric opinions and descriptions are simply "wrong," for each contains valuable psychological observations. What is wrong with them is that they do not pertain to "malingering." Thus, to take the cases cited by Eissler—whose study is psychologically the most rewarding one—it is not clear why the two men whom he describes should be considered as having "malingered": The author himself describes one as a case of severe, near-psychotic personality disorder with long-standing symptoms, and the other as a case of manifest schizophrenic psychosis. If this is so, no additional "diagnostic" labels are required.

It is important to point out, in this connection, that many psychiatrists study "malingering" without their having made such a diagnosis themselves. (This is true, for example, for Eissler's cases.) It follows, then, that someone other than the observer-author makes the diagnosis of malingering, with which the latter, in fact, might disagree, but which he accepts for purposes of classification. This is a wholly irrational procedure: It is as if a neurosurgeon were to publish a series of cases of "schizophrenia" (so diagnosed by others), all of whom proved to have suffered from various types of brain tumors.

Finally, there is a further consideration which shows us that the notion of "malingering" does not, and cannot, serve as a description either of a psychopathological syndrome" or of a particular psychological mechanism. The foregoing assertion is made in view of the fact that in military life, for example, "malingering" is spoken of only in connection with a person's alleged intention to get out of the service (or combat, etc.). It seems to me that the reverse of this is equally as common, if not more. In other words, there are many persons who enlist in the armed forces in order to get away from painful situations in their civilian home life. Many falsify information about their age, past histories, symptoms, and the like, in order to meet the requirements for enlistment. This mode of behavior, interestingly enough, is never called "malingering." Sometimes it goes by the name of "fraudulent enlistment." Needless to say, persons who do this are never prosecuted. It is clear that this whole matter is colored by the fact that service in the armed forces is considered essentially "honorable," a "patriotic duty." Therefore, no matter how someone gets into a military organization, he and his behavior are regarded as "good." By the same token, any tendency in the reverse direction, that is, away from the military organization, is considered "bad," unless mitigated by one of the socially accepted "excuses." Similarly, the feigning of health by applicants for life insurance, or by victims of Nazi concentration camps, reflects first and foremost a social structure in which a powerful incentive is placed on health, not on disease.[5] It is true that such instances often go by the term "dissimulation," to indicate the similarity to "simulation." Yet here, too, further difficulties arise, since most psychiatrists would consider the dissimulation of symptoms by victims of Nazi concentration camps as eminently healthy. This was, after all, the only way to escape death. This is considered "healthy," however, only if the psychiatrist sides with the patient's value judgment. From the point of view of the

|| References 10, 13, 17.

Nazis, it would have had to be considered "malingering," since it violated the "rules of the game" which governed life and death in the concentration camps.[7] These considerations emphasize, once again, that the notion of "malingering" tells us more about the observer's agreement or disagreement with the value judgment of the social structure in which he and the patient live than it does about the latter's behavior.

Lastly, it should be noted that "malingering" is a term which has little or no meaning in the medical (psychiatric) situation limited to two people, physician and patient. In the private practice of psychiatry, the notion of "malingering" simply fails to arise. The "Ganser syndrome" and similar psychological observations pertain to the social structure of prisons. Here the psychiatrist functions in a multibody situation,[23] involving patient, guards, wardens, and other agents of society. Similarly, in matters pertaining to insurance, the social structure in which the psychiatrist operates comprises numerous persons, and often institutions, in addition to patient and doctor. Only in the light of such considerations can the meaning of "malingering" be approached in a rational, nonjudgmental, scientific manner.

Summary

Malingering is considered in every textbook of psychiatry, and in psychoanalytic writings, as if it were a scientific concept designating a distinct mode of behavior or a psychopathological syndrome. Observations in settings where the "diagnosis" of "malingering" is sometimes made, together with study and reflection on this subject, lead to the conclusion that the aforementioned conception of "malingering" is unsound from the points of view both of semantics and of psychiatric theory. The aim of this essay is to present an analysis of the concept of "malingering," not as an alleged syndrome but as a scientific abstraction.

The exposition of this theme is divided into three parts, based on three, more or less, distinct frames of reference from which "malingering" may be viewed. We distinguish "malingering" as (1) a diagnosis; (2) a violation of a set of social rules, along the model of cheating in a game, and (3) a psychopathological syndrome characterized by special psychological features. An analysis of "malingering" in terms of each of these three points of view is presented. Particular attention is focused on an attempt to clarify, partly in terms of social structure, the various meanings of "diagnosis."

The principal conclusions of this study can be briefly summarized as follows: 1. Malingering is not a "diagnosis," in the usual sense of the word, and must be eliminated from psychiatric and medical writing as an item in the "differential diagnosis" of certain "diseases." 2. Malingering expresses the physician's moral condemnation of the patient in general, and of a specific pattern of behavior in particular. It thus tells us more about the observer (physician)—that is, his identification with the prevailing values of the social group in which he operates—than it does about the observed (patient). 3. No rational meaning can be given to "malingering" as an alleged psychopathological syndrome. It is suggested that "malingering" is best viewed in the frame of reference of the sociopsychology of games. Accordingly, this notion pertains to social situations in which the physician is a representative of some social body and plays a role analogous to that of an umpire in a competitive sport: It is his duty to make sure that no one cheats. The "malingerer" is one who cheats in a game which is a segment of "real" life.

REFERENCES

1. Balint, M.: On Punishing Offenders, in Psychoanalysis and Culture, G. B. Wilbur and W. Muensterberger, Editors, New York, International Universities Press, 1951, pp. 254-279.

2. Bleuler, E.: A Textbook of Psychiatry, translated by A. A. Brill (1924), New York, The Macmillan Company, 1944.

3. Bowman, K. M., and Rose, M.: A Criticism of Current Usage of the Term "Sexual Psychopath," Am. J. Psychiat. 109:177, 1952.

4. Bowman, K., and Rose, M.: Do Our Medical Colleagues Know What to Expect from Psychotherapy? Am. J. Psychiat. 111:401, 1954.

5. Butler, S.: Erewhon (1872), Harmondsworth, Middlesex, England, Penguin Books, Ltd., 1954.

6. Caudill, W.: Applied Anthropology in Medicine, in Anthropology Today: An Encyclopedic Inventory, A. L. Kroeber, Editor, Chicago, University of Chicago Press, 1953, pp. 771-806.

7. Cohen, E. A.: Human Behaviour in the Concentration Camp, translated by M. H. Braaksma, London, Jonathan Cape, 1954.

8. Crile, G., Jr.: A Plea Against Blind Fear of Cancer, Life 39:128 (Oct. 31) 1955.

9. Eissler, K. R.: Malingering, in Psychoanalysis and Culture, G. B. Wilbur and W. Muensterberger, Editors, New York, International Universities Press, 1951, pp. 218-253.

10. Fairbairn, W. R. D.: Psychoanalytic Studies of the Personality, with Preface by Ernest Jones, London, Tavistock Publications, Ltd., 1952.

11. Freud, S.: Leonardo da Vinci: A Study in Psychosexuality (1910), authorized translation by A. A. Brill, New York, Random House, Inc., 1947.

12. Glover, E.: Psycho-Analysis, Ed. 2, London, Staples Press, Ltd., 1949.

13. Grinker, R. R., and Spiegel, J. P.: Men Under Stress, Philadelphia, The Blakiston Company, 1954.

14. Guttmacher, M. S., and Weihofen, H.: Psychiatry and the Law, New York, W. W. Norton & Company, Inc., 1952.

15. Henderson, D., and Gillespie, R. D.: A Text-Book of Psychiatry, Ed. 7, London, Oxford University Press, 1950.

16. Langer, S. K.: Philosophy in a New Key (1952), New York, Mentor Books, New American Library of World Literature, Inc., 1953.

17. Masserman, J. H.: The Practice of Dynamic Psychiatry, Philadelphia, W. B. Saunders Company, 1955.

18. Menninger, K. A.: Man Against Himself, New York, Harcourt, Brace & Company, Inc., 1938.

19. Noyes, A. P.: Modern Clinical Psychiatry, Ed. 3, Philadelphia, W. B. Saunders Company, 1948.

20. Parsons T.: Illness and the Role of the Physician: A Sociological Perspective, Am. J. Orthopsychiat. 21:452, 1951.

21. Parsons, T.: Social Structure and Dynamic Process: The Case of Modern Medical Practice, in The Social System, Glencoe, Ill., The Free Press, 1952, Chap. X, pp. 428-479.

22. Radin, M.: The Law and You (1948), New York, Mentor Books, New American Library of World Literature, Inc., 1955.

23. Rickman, J.: Number and the Human Sciences, in Psychoanalysis and Culture, G. Wilbur and W. Muensterberger, Editors, New York, International Universities Press, 1951, pp. 150-155.

24. Schneider, D. M.: The Social Dynamics of Physical Disability in Army Basic Training, Psychiatry 10:323, 1947.

25. Szasz, T. S.: Psychiatric Expert Testimony: Its Covert Meaning and Social Function, Psychiatry, to be published.

26. Szasz, T. S.: Some Observations on the Relationship Between Psychiatry and the Law, A. M. A. Arch. Neurol. & Psychiat. 75:297, 1956.

27. Wertham, F.: Dark Legend, New York, Doubleday & Company, Inc., 1949.

28. Wertham, F.: The Show of Violence, New York, Doubleday & Company, Inc., 1949.

The in Vitro Oxidation of Epinephrine in Plasma

BYRON E. LEACH, Ph.D.
and
ROBERT G. HEATH, M.D., New Orleans

Introduction

Several reports have recently appeared in the literature which speculate on the possibility that faulty epinephrine metabolism might underlie the psychological aberrations that one sees in schizophrenic patients. Lindemann [1] reported aggravation of psychotic symptoms in schizophrenic patients following injections of epinephrine. Hoffer * and Osmond,[3] in several articles, mention this possibility and describe the appearance of psychotic-like symptoms in normal persons following the administration of adrenochrome and adrenolutin (3,5,6-trihydroxy-1-methylindole), two oxidation products of epinephrine metabolism. Rinkel and associates [4] speculate upon the possibility that adrenoxine, another oxidation product of epinephrine metabolism of yet unknown structure, may be the responsible agent in the production of psychotic symptoms. In the monograph, "Studies in Schizophrenia,"[5] we described aberrations on physiological recordings in the septal region and hippocampus which occur consistently in schizophrenic patients. Stimulation of the septal region produced autonomic changes similar to those seen with the administration of epinephrine. From these observations we speculated that perhaps this region of the brain might assert some control over epinephrine metabolism.

On the basis of these observations a procedure was devised to test the effects of the interaction of human plasma or serum with epinephrine in vitro in an attempt to determine whether the plasma or serum of schizophrenics reacted differently with epinephrine from the plasma or serum of normal persons. In this report we shall present our findings, which suggest a significant quantitative difference in the speed of epinephrine oxidation in the two groups. However, this phenomenon appears to be nonspecific, since it occurs in association with diseases other than schizophrenia.

Method for Measuring in Vitro Oxidation of Epinephrine in Plasma or Serum

The rate of oxidation of epinephrine in the presence of plasma or serum was measured in a Beckman DK recording spectrophotometer between wave lengths of 300 and 600 mμ. The spectrophotometric method was chosen to measure oxidation in preference to the Warburg technique because we were interested not only in whether increased oxidation occurred but also in gathering information concerning the nature of the specific oxidation products which were formed. Fasting blood was drawn from the antecubital vein, heparinized, and the plasma separated immediately (serum reacts in the same manner). As a general rule the plasma was used within a two-hour period. Since the rate of oxidation of catecholamines, such as epinephrine, is markedly affected by very small changes in pH, the plasma or serum was first neutralized with hydrochloric acid to remove the excess bicarbonate. It is also very important that the molarity of the phosphate buffer be maintained at a constant value. For the actual spectrophotometric determination, the following procedure

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From the Department of Psychiatry and Neurology, Tulane University of Louisiana School of Medicine, and Charity Hospital of Louisiana.

* Hoffer, A.: Adrenolutin as a Psychomimetic Agent, read at the combined meeting of the American Physiological Society and the American Association for the Advancement of Science, Atlanta, Dec. 27, 1955. Hoffer, Osmond, and Smythies.[2]

was rigidly employed for each set of determinations.

The blank tube contains 1 ml. of plasma or serum, 1 ml. of 0.03 N hydrochloric acid and 1 ml. of 0.5 M phosphate buffer (pH 7.40). The experimental sample tube contains 1 ml. of plasma or serum, 1 ml. of 0.5 M phosphate buffer (pH 7.40) and 1 ml. of 2 mg/ml. solution of epinephrine. The epinephrine is prepared fresh each day by dissolving 50 mg. of epinephrine base in 25 ml. of 0.03 N hydrochloric acid. The contents of each tube are mixed thoroughly: The solution in the blank tube is transferred to the reference cell and the contents of the experimental tube to the sample cell. The spectrum is recorded immediately between 600 and 300 mμ. To record the spectrum from 600 to 300 mμ, using scanning speed 3, requires approximately four minutes. After scanning the solutions are transferred from the Beckman curvettes to large test tubes, placed in a water bath at 37 C and shaken in contact with air for approximately 75 minutes. At exactly 80 minutes after the epinephrine has been added to the experimental tube, the spectrum is superimposed on the recording obtained initially. The difference between the 80-minute tracing and the initial tracing at 395 mμ is recorded. The optical density difference at 395 mμ is used throughout for all calculations.

Results

Normal Persons.—The data on a series of 20 normal subjects free of systemic disease selected from members of the staff are summarized in Table 1. The group included 16 men and 4 women. A total of 77 curves were followed on these subjects. The number of determinations on each subject varied from 2 to 13. Duplicate samples were run on several of these determinations, and in none of these instances was the variation as great as 5%. The mean value of the optical density at the 395 mμ peak between the 80-minute curve and the initial curve was 0.108, with a standard deviation of ±0.047. The over-all range for all subjects regardless of the number of curves was 0.030 to 0.225. Figure 1 demonstrates the type of absorption curve obtained for the normal subject. The highest average optical density for a subject (No. 4) in this group was 0.175.

TABLE 1.—*Oxidation of Epinephrine in Vitro in Plasma of Controls*

Subject	Sex	No. of Determinations	Optical Density Difference at 395 μ Peak After 80 Min.	
			Average	Range
1	M	5	0.116	0.070–.170
2	M	7	0.131	0.040–.200
3	M	13	0.055	0.035–.100
4	F	5	0.175	0.130–.225
5	M	2	0.160	0.130–.190
6	M	3	0.155	0.115–.135
7	M	4	0.081	0.055–.115
8	M	3	0.152	0.075–.215
9	M	4	0.088	0.035–.165
10	M	5	0.084	0.055–.130
11	M	3	0.088	0.070–.100
12	M	2	0.030	0.030–.030
13	M	3	0.032	0.030–.035
14	F	3	0.095	0.055–.125
15	F	4	0.127	0.100–.185
16	F	3	0.162	0.120–.200
17	M	2	0.170	0.160–.180
18	M	2	0.040	0.035–.045
19	M	2	0.160	0.155–.165
20	M	2	0.050	0.045–.055
		77 Total	Mean 0.108 ±0.047	0.030–.225 Over-All Range

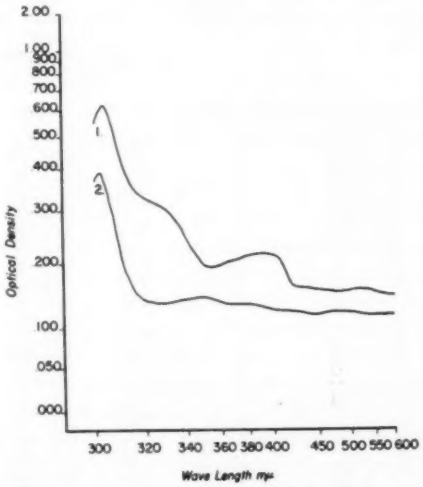

Fig. 1.—Spectra showing the oxidation of 2 mg. of epinephrine in the presence of 1 ml. of plasma of a normal subject at 1 min. (*1*) and 80 min. (*2*) at 37 C.

Schizophrenic Patients.—The data on this series of patients are summarized in Table 2. Subjects in this group were hospitalized schizophrenic patients who were not receiving physical therapy or drugs. Care was taken to select only persons in good physical condition with a negative history for recent infectious disease. Patients fitting into all subclassifications of schizophrenia were included, since these diagnostic entities ap-

TABLE 2.—*Oxidation of Epinephrine in Vitro in Plasma of Psychotic Patients Not on Medication*

Patient	Sex	No. of Determinations	Optical Density Difference at 395 mμ Peak After 80 Min.	
			Average	Range
1	F	3	0.168	0.095–.235
2	F	3	0.260	0.200–.310
3	F	3	0.220	0.135–.315
4	F	3	0.220	0.155–.260
5	F	4	0.126	0.075–.185
6	F	2	0.140	0.120–.160
7	F	3	0.158	0.130–.185
8	F	2	0.245	0.130–.360
9	F	4	0.240	0.140–.420
10	F	5	0.315	0.200–.515
11	F	4	0.209	0.190–.245
12	F	4	0.181	0.100–.290
13	F	3	0.178	0.120–.215
14	F	2	0.270	0.240–.300
15	M	3	0.138	0.055–.195
16	M	2	0.433	0.365–.500
17	M	3	0.153	0.100–.235
18	M	2	0.053	0.035–.070
19	M	3	0.402	0.285–.510
20	F	2	0.208	0.170–.245
21	F	3	0.092	0.025–.155
22	F	4	0.716	0.695–.800
23	F	4	0.225	0.175–.275
24	F	4	0.436	0.355–.630
25	F	4	0.188	0.105–.330
26	M	6	0.316	0.200–.500
27	F	4	0.434	0.360–.520
28	F	4	0.235	0.065–.435
29	F	4	0.178	0.110–.220
30	M	3	0.035	0.030–.045
31	F	5	0.207	0.107–.320
32	M	4	0.274	0.200–.360
33	M	4	0.281	0.215–.335
34	M	7	0.150	0.045–.335
35	M	3	0.243	0.200–.280
36	F	3	0.323	0.255–.460
37	F	3	0.295	0.290–.305
38	F	3	0.340	0.250–.400
39	M	4	0.103	0.040–.215
40	M	2	0.230	0.190–.270
41	M	3	0.427	0.325–.540
42	M	4	0.410	0.280–.515
43	M	6	0.554	0.335–.700
44	M	12	0.275	0.000–.660
	17 Males 27 Females	163 Total	Mean 0.257 ±0.130	0.030–.800 Over-All Range

parently could not be correlated with the variations in the readings obtained. The duration of illness in this patient group varied widely. There were 44 patients in this group, including 17 males and 27 females. They varied in age from 16 to 70 years. There was no correlation between these factors and findings on the test. Each patient was tested on 2 to 12 different days, giving a total of 163 curves. The mean optical density difference between the immediate and the 80-minute curves at 395 mμ for this group was 0.257±0.130. A typical absorption curve for the patient group is shown in Figure 2. The over-all range was 0.030 to 0.800.

It can be seen by comparing the two groups, Table 1 and Table 2, that there is overlapping. It is not uncommon to find a patient in the optical density range of 0.175 or below, where the majority of normals fell. There are 11 out of the 44 schizophrenics in the group whose average optical density at 395 mμ was in this range. There are, however, only four patients whose average curve was below the mean for the normal group, of 0.108. It is also significant to note that the over-all range for the psychotic group is extremely wide; in fact, the values for the individual subject do not stay at all constant. For example, tests on Patient 44 have been run at intervals for more than a year, and the variations are 0.060 to 0.660.

The differences between the two groups, the normals and the psychotics, are significant statistically at the 1% level, in spite of the fact that the two groups overlap.

Chronic Hospitalized Patients Without Psychosis.—The data on this group of patients are summarized in Table 3. Patients with some diseases not associated with pathological behavior have shown optical densities above that usually seen in nor-

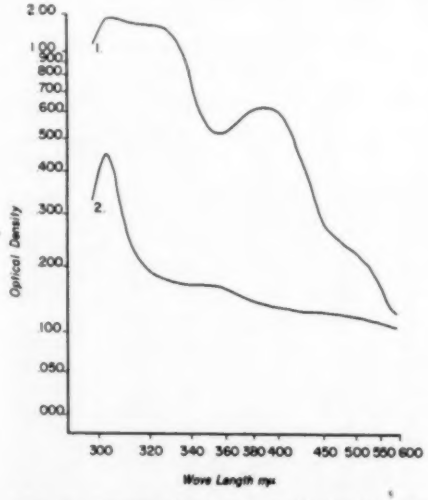

Fig. 2.—Spectra showing the oxidation of 2 mg. of epinephrine in the presence of 1 ml. of plasma of a schizophrenic at 1 min. (*1*) and 80 min. (*2*) at 37 C.

TABLE 3.—*Oxidation of Epinephrine in Vitro in Plasma in Various Diseases Other Than Schizophrenia*

Subject	No. of Determinations	Optical Density Difference at 395 mμ Peak After 80 Min.		Comments
		Average	Range	
A	3	0.140	0.130–.150	Anemia
B	3	0.308	0.255–.355	Congestive heart failure
C	4	0.155	0.150–.165	Leukemia
D	3	0.342	0.270–.430	Malignant hypertension
E	4	0.636	0.460–.745	Terminal bronchiogenic cancer
F	3	0.097	0.030–.150	Parkinson's disease
	6*	0.151	0.085–.175	Tuberculosis
	6*	0.184	0.130–.315	Postacute infection

* This is an average of six patients, instead of one subject, as is the case with all the others.

mals. Consistently this is seen in association with chronic infections and terminal malignancies and during the convalescent period from acute infectious processes.

In addition to the group of patients hospitalized for chronic illness, several members of the staff who had been used as normal controls were followed, determinations being made during and immediately following acute respiratory illness. In these persons the speed of oxidation was increased significantly for periods up to 10 days following disappearance of fever. In all subjects in whom the speed of oxidation was increased, there was found to be an elevated erythrocyte sedimentation rate. In all instances the elevated sedimentation rate persisted beyond the period in which the speed of oxidation was increased.

Results in Association with Foreign Protein Reaction.—The test was administered to one of the normal subjects (Table 4) in conjunction with his receiving tetanus antitoxin for a cat bite. Twenty-four hours after receiving the antitoxin, the subject showed a significant increase in the oxidation of epinephrine in this time period from 0.035 to 0.260. After 30 hours the optical density fell into the normal range but still remained slightly above the pre-antitoxin level. Epinephrine, 0.3 mg., was then administered intramuscularly, and 45 minutes later the optical density fell to approximately the level present before antitoxin was administered. Approximately five weeks later the subject was given toxoid. Following this the optical density again increased, but to a slighter degree than following the first antitoxin innoculation. A second toxoid injection, six weeks later, again produced a temporary, but still less marked, increase.

Effects of Addition of Copper Sulfate and Sodium Cyanide to Plasma on Epinephrine Oxidation Curves

Tests have been carried out in an effort to gain additional information on the nature of the substance in the plasma which might play a role in the epinephrine oxidation. Reports in the literature suggest that various compounds, when added to serum, do accelerate or inhibit the oxidation of

TABLE 4.—*Effect of Tetanus Antitoxin and Tetanus Toxoid on in Vitro Oxidation of Epipephrine in Plasma*

Subject	Date	Optical Density Difference at 395 mμ Peak After 80 Min.	Comment
3	6/22/55	0.035	Before tetanus antitoxin
3	6/23/55	0.260	24 hr. after tetanus antitoxin
3	6/23/55	0.060	30 hr. after tetanus antitoxin
3	6/23/55	0.045	31 hr. after tetanus antitoxin and 40 min. after 0.3 mg. epinephrine I.M.
3	7/27/55	0.095	Before tetanus toxoid
3	7/27/55	0.185	6 hr. after tetanus toxoid
3	7/28/55	0.095	24 hr. after tetanus toxoid
3	7/28/55	0.050	30 hr. after tetanus toxoid
3	9/ 7/55	0.035	Before tetanus toxoid
3	9/ 7/55	0.100	6 hr. after tetanus toxoid
3	9/ 8/55	0.040	24 hr. after tetanus toxoid

catechol. Shacter[6] reports that the cupric ion accelerates oxidation, whereas the cyanide ion inhibits the oxidation of catechol. Plant tyrosinase, a known oxidizing enzyme for tyrosine as well as catechol, is known to contain copper. On the basis of these reports, it was speculated that perhaps a copper-containing enzyme might be responsible for the increased speed of oxidation which we found in our patient group. Therefore, the effect of adding copper to this reaction mixture was tested. Also, on the basis of Shacter's report, the addition of sodium cyanide was also tested to determine whether it would inhibit this particular reaction. The results are summarized in Table 5. Cupric ion at concentrations of 5×10^{-5} and 5×10^{-6} m markedly increased the oxidation of epinephrine in the presence of plasma, whereas the cyanide at concentrations of 5×10^{-4} m inhibited the oxidation of epinephrine in this reaction.

TABLE 5.—*Effects of Sodium Cyanide and Copper Sulfate on in Vitro Oxidation of Epinephrine in Plasma*

Subject	Date	Optical Density Difference at 395 mμ After 80 Min. Standard Procedure	Amount of $CuSO_4$ Added	Optical Density Difference at 395 mμ After 80 Min. with Added $CuSO_4$	Amount of NaCN Added	Optical Density Difference at 395 mμ After 80 Min. with Added NaCN
A	11/ 1/55	0.035	5×10^{-4} M	0.120	5×10^{-4} M	0.00
B	11/16/55	0.265	5×10^{-4} M	1.000		
C	11/16/55	0.645	5×10^{-4} M	1.300		
C	11/18/55	0.840			5×10^{-4} M	0.155

characteristics on the spectrophotometer: maxima at 301 and 489 mμ; minima at 260 and 362 mμ.

When 10 γ of adrenochrome, instead of the 2 mg. of epinephrine base conventionally used in the procedure, was added to plasma or serum, the immediate curve was the same as that obtained with adrenochrome alone. Eighty minutes later, however, the adrenochrome was almost completely converted to the product exhibiting a peak at 395 mμ. This conversion, however, took place within a period of less than 20 minutes, a rate much faster than was ever obtained when epinephrine was mixed with the plasma or serum. Figure 3 illustrates the type of spectra obtained when adrenochrome is added to the plasma, and should be contrasted with Figures 1 and 2, where epinephrine was added to plasma from the normal and schizophrenic patients, respectively. This suggests that the important rate differences between the normal group and the patient group in amount of oxidation of epinephrine take place in the conversion of epinephrine to adrenochrome. On all of the oxidation curves it will be noted that, in addition to the compound formed at 395 mμ, there is also a shoulder observed at 490 mμ. This is consistently more apparent when the oxidation is above the normal range.

Results Obtained with Substitution of Adrenochrome for Epinephrine in Test Procedure

In the oxidation of epinephrine, adrenochrome is known to be one of the compounds formed. In an effort to gain additional information as to the possible nature of the breakdown products formed during this test procedure, adrenochrome was added to the serum or plasma instead of epinephrine and the absorption spectra were followed in the same manner. The adrenochrome used in this study was prepared from *l*-epinephrine by the method described by Schayer.[7] Adrenochrome prepared in this manner exhibits the following

Comment

It is apparent from these data that in the absence of systemic disease the speed of oxidation of epinephrine by plasma is significantly greater in the schizophrenic than

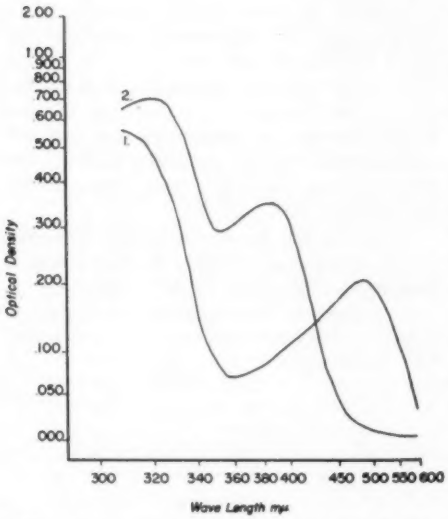

Fig. 3.—Spectra obtained at 1 (*1*) and 80 min. (*2*) for Patient C with the addition of adrenochrome to plasma.

in the normal group, as measured by the method described. There is, however, some degree of overlapping between the two groups. The test results in patients with diseases other than schizophrenia indicate that this phenomenon is not specifically related to schizophrenia. It occurs in association with various types of bodily insult, and this suggests it may be related to defense reactions on the part of the body. This is supported by the fact that other tests which indicate defense reactions on the part of the body, such as the sedimentation rate and serum globulin, were usually also increased in the patients with diseases other than schizophrenia who showed increased speed of oxidation.

Although the spectrum reading suggests the formation of a specific compound, as indicated by the sharp, rather well-defined peak at 395 mμ, we as yet have not been able to identify this compound. It is not adrenochrome, which has different spectrum characteristics (Fig. 3). We have no information which could indicate whether it is or is not one of the other oxidation products which have been suggested as being responsible for the appearance of psychotic symptoms. Since, however, patients without psychosis show this increased peak, it is illogical to assume that this oxidation product per se is specifically related to the appearance of psychotic symptoms.

These findings suggest that in schizophrenia, as well as in the other disease processes which are associated with this change, there is either an increase in the amount of oxidizing enzyme or a diminution in the amount of an endogenous inhibitor in the serum. The studies whereby the addition of cupric ion increased oxidation and the addition of cyanide reduced oxidation suggested the possibility that in schizophrenia, as well as in other disease processes showing the phenomenon of increased oxidation, there might be higher levels of a circulating copper-containing enzyme. We have investigated this possibility, and the findings will be presented in a separate report. Another possibility to be considered is that there might be a qualitative difference in the copper-containing enzyme between the schizophrenic and the nonschizophrenic group with increased oxidation. This would thus account for the behavioral abnormalities being present in schizophrenia, but not in the other diseases.

Summary

A spectrophotometric method for testing in vitro the oxidation of epinephrine by plasma of humans is described.

In the absence of systemic disease, plasma from schizophrenic patients produced faster oxidation of epinephrine than does the plasma from normal subjects. This finding in schizophrenics, however, appears to be a nonspecific reaction, since the same phenomenon is encountered when serum or plasma from patients with a variety of acute and chronic disease processes is similarly tested.

It is speculated, on the basis of the manner in which the cupric ion and cyanide ion affect the oxidation curves, that schizophrenia, as well as some other disease processes, is associated with increased quantities of copper-containing enzyme. The

possibility is entertained that there is a qualitative difference in this enzyme between schizophrenics and persons without psychotic behavior.

REFERENCES

1. Lindemann, E.: Psychopathological Effect of Drugs Affecting the Vegetative Nervous System: Adrenalin, Am. J. Psychiat. 91:983, 1935.

2. Hoffer, A.; Osmond, H., and Smythies, J.: Schizophrenia: A New Approach, J. Ment. Sc. 100:29, 1954.

3. Osmond, H.: Inspiration and Method in Schizophrenia Research, Dis. Nerv. System 16:101, 1955.

4. Rinkel, M.; Hyde, R. W.; Solomon, H. C., and Hoagland, H.: Experimental Psychiatry: II., Am. J. Psychiat. 111:881, 1955.

5. Tulane University School of Medicine, Department of Psychiatry and Neurology: Studies in Schizophrenia: A Multidisciplinary Approach to Mind-Brain Relationships, Robert G. Heath, and others, Editors, Cambridge, Mass., Harvard University Press, 1954.

6. Shacter, B.: Serum Catecholase: Properties of the Enzyme and Nature of an Endogenous Inhibitor, J. Biol. Chem. 184:697, 1950.

7. Schayer, R. W.: Synthesis of *dl*-Adrenalin-β-C^{14} and *dl*-Adrenochrome-β-C^{14}, J. Am. Chem. Soc. 74:2441, 1952.

Books

Hypnotic Suggestions. By S. J. Van Pelt, M.B., B.S. Price, $2.75. Pp. 95. Philosophical Library, Inc., 15 E. 40th St., New York, 1956.

The Nature of Hypnosis. By Paul Schilder, M.D., Ph.D.; translated by Gerda Corvin. Price, $4.00. Pp. 204. International Universities Press, Inc., 227 W. 13th St., New York, 1956.

With today's interest in hypnosis ranging from its use in childbirth without anesthesia to a review of Freud's early contributions (on the occasion of the centenary of his birth), two books have been published on the subject that are most timely.

Van Pelt, president of the British Society of Medical Hypnotists, has written a slim volume addressed to general medical practitioners and psychiatrists, in which his general thesis is that hypnotic suggestion plays a major role in the etiology and treatment of psychoneuroses, and that one can achieve much success in treatment of neuroses by suggestion, using only a light state of hypnosis, according to principles of "relaxation, realization, and reeducation." He feels that "units of mind power" can be made to carry "doses of suggestion," that in hypnosis the mind is concentrated, and thus suggestion can be effective. He states that the force used is the subject's own imagination, and that hypnotism is a manipulation of it.

The book is thorough, brief, readable, with extensive references. It reviews the phenomena of hypnosis, and methods of inducing it, emphasizing the brevity of therapy and describing hypnosis as "a scientific, medical, and therapeutic procedure."

He states that "naturally-occurring" neuroses are a result of accidental self-hypnosis and suggestion, perpetuated by fear, tension, and secondary symptoms. "An emotional incident or idea is thought to concentrate in the mind, producing a condition of hypnosis, and any idea or thought then introduced acts as a hypnotic suggestion, so that a psychoneurosis is, to all intents and purposes, the same in its structure as the behavior and symptoms arising from a hypnotic or post-hypnotic suggestion." The author is not much out of step with dynamic psychiatric thinking except where he postulates that traumatic events act like hypnotic suggestion. (Just because neuroses and hypnotic suggestion can demonstrate the same symptomatology does not mean they are etiologically related.)

In treatment, he uses relaxation, realization, and reeducation plus hypnosis, a method which seems to consist chiefly of guidance, persuasion, support, minimal abreaction, and superficial interpretation. He rightly minimizes symptoms and suggests that to cure one must go to the root of the trouble. He presents twelve illustrative case histories of patients with symptom neuroses and states he is able to get them to recall their basic conflicts under light hypnosis, usually in the third hour, and by the sixth to the twelfth hour they have become essentially well. One wonders if the crucial memory may be a distortion, or too superficial to be of basic value, or if the recall, by changing the defensive structure, might not precipitate panics or psychoses. One wonders how these patients manage to improve without any real working through of the conflictual material. Or is the symptom given up to please the permissive doctor, in a hypnotic situation of relaxation and rapport?

All in all, this is an interesting little book, and those who are impressed with hypnosis will be impressed by it, and those who are not, will not.

Schilder's book is a new English translation of two monographs, "The Nature of Hypnosis," published in 1921, and "A Textbook of Hypnosis," put out by Schilder and Otto Kauders in 1926. The former was never translated before, and the latter has been out of print for many years. This book is of both intrinsic and historical value. It discusses principles, values, limitations, theory, and special problems of hypnosis as a therapeutic technique, making significant contributions to psychosomatic problems, narcohypnosis, psychoanalysis, and perceptual psychology. It is thoughtful, original, and stimulating. It is particularly impressive because it might have been written yesterday, although the material is over thirty years old.

Schilder tries to locate the hypnotic effect in certain subcortical centers. He feels the hypnotizable person has an unconscious wish for sleep, that up to a point the subject becomes hypnotized for the sake of the doctor. He sees the hypnotic state as a partial regression to an erotic, masochistic, and submissive state. The hypnosis represents the pleasure of surrender, and a sharing of the creative power of the hypnotist via identification. The subject

therefore produces a hypnotic state out of his own emotional needs, the doctor acting as an object around which regression occurs to a narcissistic level, representing magic through a revival of an omnipotent parental image.

Schilder discusses the affects and suggestion of affects in hypnosis and their effects on bodily functions. This is significant for current psychosomatic concepts. Hypnotism is seen as affecting the phylogenetically deeply rooted vasovegetative system, and thus is an archaic regressive phenomenon in both psychological and physiological terms. He speaks descriptively of the sleeper as having a waking, a sleeping, and a dream ego. He attempts to explain many manifestations of hypnosis on the basis of the psychology of sleep, a thesis that Van Pelt denies. Unfortunately, a discussion of all the areas of conflict between the two authors is beyond the scope of this review. The degree of suggestive rapport between doctor and subject is related to the degree of control of the subject by his own ego ideal, thus stressing the limitations of the doctor's power, such as the inability of a hypnotist to make a subject commit a crime he would not ordinarily do. The amnesia in hypnotism is seen as due to affective experiences, and thus is like forgetting in general.

There is a detailed discussion of techniques, values, limitations, and inherent dangers, and Schilder is very cautious in his positive recommendations. This book will be of value to and enjoyed by those interested not only in hypnotism, but also in many other phenomena of human behavior and dynamics, such as sleep and amnesia.

Psychotherapy and Counseling. By Lawrence K. Frank and Rollo May (Conference Co-Chairmen), F. H. Allen, L. N. Austin, P. David, P. E. Johnson, G. A. Kelly, E. Lindemann, N. Mailloux, T. F. McNair Scott, W. E. Oates, H. H. Perlman, W. G. Perry Jr., N. Sanford, R. W. White, L. E. Woodward, and P. Zlatchin. Ann. New York Acad. Sc., Vol. 63, Art. 3, Pp. 319-432, New York Academy of Sciences, 2 E. 63d St., New York 21, 1955.

This is the report of a conference of five professions active in the field of psychotherapy and counseling. At the broadest level the purpose was "to describe the current common accepted practice by which each of these professions (medicine, psychology, social work, the ministry, and counseling and guidance) seeks to meet those human needs that can be helped by psychotherapy and counseling, however designated, and to describe also the particular training now being provided." Commissions of five to eight members of each profession met for many months to formulate their thoughts on such specific issues: the type of problem and patient best treated by the profession; the methods used; the selection, training and supervision of their practitioners; the conditions for collaboration between theirs and other disciplines; the social sanctions and expectations which influence their functions and practice, and the methods by which their work is critically examined and professional competence advanced. The monograph consists of the reports of the five commissions and a number of commenting statements on each by other professionals in the field.

The most informative and complete discussions are by the groups in psychology and social work. Both approached the problems raised by the conference thoughtfully and gave detailed opinion of each of the specific issues. For the medical reader who may have limited contact with these professions, here is an opportunity to obtain a clear picture of the professional self-concept of these fields in their treatment function. The Commission of Counseling and Guidance focuses its report on the distinction between counseling and psychotherapy. The ministers, to whom counseling is an age-old function but only recently of self-conscious concern, point their discussion toward the understanding of the possible conflicts in the joint roles of minister and counselor and to the coordination of religious and psychotherapeutic values.

Unfortunately, the Commission on Medicine, comprised of psychiatrists, an internist, an orthopedist, and a pediatrician, produced the slimmest and, on a number of counts, the most superficial report. It barely treats any of the major problems of psychiatry. Selection and training of psychiatrists, the understanding of psychodynamics and psychopathology, the development and evaluation of treatment methods, and the relation to nonmedical professions in the treatment function are almost entirely neglected questions. Rather, it develops as its major emphasis the need for physicians of all specialties to be sensitive to their patients' emotional needs, to understand the patient as a person, and to recognize the psychotherapeutic relation inherent in the physician-patient transaction whatever the disease treated. The need for the diffusion of psychiatric thinking throughout the entirety of medical practice is convincingly argued and, judging from the comments of nonpsychiatric physicians, is daily gaining acceptance in many branches of medicine. But little is added by the report to an understanding of the unique function of psychotherapy within the psychiatric specialty.

The human problems with which psychotherapy and counseling are concerned range from the one extreme of those which are largely intrapsychically determined, derived from early character development, and dependent upon the action of unconscious processes, to the other extreme of role adaptation problems, mainly in the client's contemporary social life. The Commission on Counseling and Guidance suggests that psychotherapy and counseling may be distinguished in terms of this continuum: psychotherapists, trained in psychodynamics and psychopathology, working with intrapersonal conflict problems, with "the dynamics considered with emphasis on projection on the therapist," and having the final goal of personal integration and mental health; the Counseling group, with training in psychodynamics and having knowledge of the particular role-area (e.g., work), working with clients' more circumscribed role problems, with the goal of creating competence in the given area. The transition between the two approaches is gradual, but viewing psychological problems, and hence their treatment by different specialties, along such a dimension is of value. Understanding the vicissitudes of the labor market rather than those of the unconscious may be of greater importance in vocational counseling, and the client's adjustment may be materially advanced by direct guidance and information. Still other dimensions emerge in these reports. Individuals' psychological problems differ in the degree to which they are part of a psychosomatic field, closely tied to biological disease processes, or a psychosocial field, involving family, community, or church. Similiarly, they differ in their profoundity, in the specificity or generality of their crippling effects, and in their social consequences.

Consequently, the monograph as a whole leads inescapably to the conclusion that each of the disciplines, and perhaps others, must share in the challenging task of relieving psychological suffering. Each profession, with its particular tradition and training, has considerable to contribute, perhaps in an area of special competence, and much to learn from the others. As Lawrence Frank points out in his final summary, each of the professions is aware that the basic training of its field (M.D., Ph.D., D.D., or whatever the title) is insufficient for the work of psychotherapy and counseling. There is a readiness to learn and, equally, to unlearn. Perhaps of greatest importance is the underlying conviction that human nature can be helped to develop and improve. Throughout there is "an assertion that various kinds of dysfunctions, self-defeat, and warping can be reversed under appropriate care and treatment." And paralleling this belief is the equally strong faith that the methods of scientific inquiry can and must be used in the continued development of rational methods for the treatment of personality distortions.

A Scientific Report on "The Search for Bridey Murphy." Edited by Milton V. Kline, Ph.D. Pp. 234. Julian Press, Inc., 251 4th Ave., New York 10, 1956.

Since Mr. Morey Bernstein has written a headline-making book for public consumption entitled "The Search for Bridey Murphy," his fantasies have stirred up the lay public to even greater imaginations regarding the possibility of reincarnation. More than that, many psychiatrists have been besieged for their opinions by the public and have encountered numerous requests for hypnotic treatment. It is, therefore, a happy circumstance that six members of The Society for Clinical and Experimental Hypnosis quickly compiled an authentic scientific report on "The Search for Bridey Murphy." The authors are all serious and experienced investigators in the field of hypnosis. They consider the problems of medical hypnosis, of reincarnation, of the relationship between the hypnotist and his subject, of ostensibly supernatural phenomena, and the meaning of hypnotic behavior. They have produced an outstanding work, which adequately refutes the naïve assertions of the inexperienced Bernstein. They adequately describe his need to imitate the power and domination of the hypnotist over his patient. After thoroughly analyzing the tape recordings of Ruth Simmons, they point out convincingly her efforts to deny Bernstein's commands for her to develop a personality of an individual living in a previous generation. She loses the struggle and to the best of her ability produces what he wants.

This book is recommended to psychiatrists but may also be understandable by the intelligent lay person, and psychiatrists may wisely suggest this book to those who want to know more about the facts of hypnotism.

Police Drugs. By Jean Rolin: translated by Laurence J. Bendit. Price. $4.75. Pp. 194. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1956.

The author states that he is an academician, but other than that we know nothing

about his particular specialty. He apparently became incensed at the use of a drug in the famous French Cens case. As a result, he has written an angry diatribe against the use of drugs by the police in order to obtain confessions and against medical legal testimony by psychiatrists on the basis of what has been discovered through narcoanalytic procedures. From this one case he discusses the ethical, moral, and spiritual problems of all drug administration, including sleeping tablets and "pep" pills. The book should be read by all psychiatrists, since pharmacotherapy is utilized by all of them at one time or another. It brings home to the reader the moralistic problems and extends the problem of drugs into the realm of philosophy, individual dignity, and freedom for self-realization. Even though it is an angry book, containing much abuse of the medical profession, some of which is no doubt deserved, it is very much worth-while reading.

Great Men—Psychoanalytic Studies. By Edward Hitschmann, M.D., with foreword by Ernest Jones, M.D. Price, $4.00. Pp. 278. International Universities Press, Inc., 227 W. 13th St., New York 11, 1956.

Dr. Hitschmann and Dr. Ernest Jones are the oldest living exponents of Freud's work. Hitschmann very early became interested in the nature of creative processes viewed from the psychoanalytic frame of reference. He brought to this method a high quality of scholarship and artistry. This is clearly pointed out in an excellent preface by Dr. Sydney Margolin. The great men studied by Hitschmann through the psychoanalytic method include Schopenhauer, Samuel Johnson, Boswell, and several others. His writings concerning great men, dating from about 1911 through 1951, have been translated into English and collected in this volume. The individual essays make fascinating reading, and, although one may decry the lack of data on which conclusions were made and the strictly psychoanalytic point of view, nevertheless, the total volume makes for fascinating and constructive reading.

Centennial Papers. Saint Elizabeth's Hospital, 1855-1955. Winfred Overholser, Editor. Price, $3.50. With 8 illustrations. Centennial Commission, St. Elizabeth's Hospital, Nichols Ave., S.E., Washington, D. C., 1956.

One hundred years of psychiatry in the United States are rolled before the reader's eyes in this volume of papers. The total makes fascinating reading for the contemporary psychiatrist who is receptive to the story of the vicissitudes of his profession and the great men who worked under early and primitive circumstances. In this account special attention is given to William A. White, who was responsible for so many modern advances, although all five of the past superintendents are thoroughly appreciated, including the present incumbent, Winfred Overholser. Additional papers include discussions of psychiatry in Spain, France, Germany, and England. Also there are informative discussions of various branches of modern psychiatry by recognized contemporary authorities. This is truly an instructive book, and one that should have an honored position in the psychiatrist's library.

The Hostile Mind: The Sources and Consequences of Love and Hate. By Leon J. Saul, M.D., Professor of Clinical Psychiatry and Chief of the Section of Preventive Psychiatry, University of Pennsylvania School of Medicine; Psychiatric Consultant to Swarthmore College. Price, not given. Pp. 211. Random House, Inc., 457 Madison Ave., New York 22, 1956.

The author addresses himself to the general public in the interests of presenting current psychiatric knowledge about the "central problem in human affairs"—hostility. In simple terms and literate style, this brief book achieves the goal of presenting much of the opinion arising from the ego and social psychology wings of the psychoanalytic flying machine. The central idea is straightforward: Hostility, the tendency to injure others, is a fundamental component in all psychopathology; make people emotionally mature, and the problems of criminality, antisocial political action, wars, and anything else which may be characterized as destructive of man will all tend to disappear.

Part One, the Biological Orientation, defines hostility and traces the fight-flight reflex in animals and man. It is brief and general. Part Two is concerned with hostility as a disease. Here the central idea noted above is exposed. The flavor of this section of the book may be shown by mention of some of the authors mixed into it: Suttie; Adler; Ferenczi; the "Authoritarian Personality" folks, Freud ("Civilization and Its Dis-

contents"), A. Freud, and Burlingham, and the anthropologists Benedict and Mead. Clearly, psychopathology and its offspring, hostility, is a socially determined phenomenon in this book. Part Three is concerned with various manifestations of the handling of hostility: the antisocial; the private, or neurotic; the psychosomatic, and the sublimated, or social forms. These are described more fully, with case histories used to clinch the matter. Part Four handles hostility and everyday sorts of things, such as politics, religion, and happiness. (This is the weakest portion of the book. Neurosis has something to do with one's political beliefs, but it is far from the whole story.) Part Five, the climax, is titled "Cure and Prevention," and it amounts to the plea for all of us to make parents bring up their children properly.

Three points may be sufficient to illuminate the sorts of discontent an enlightened reader might feel. First, eclectics, if they are to maintain their position, must deny the crucial conflicts among the authors they lean upon, and these areas of theoretical conflict are always of major importance. While one may not wish to see partisan struggles thrown at the general public, nevertheless, the loose thinking that acts as if different psychologies are all describing reality in the same way is to be deplored. The author might well have turned out a superior product if he had developed the ramifications of his own theory of emotional maturity without calling upon so many diverse experts.

Second, the psychological scientist must deny that the precepts of current religion and of psychology in general are as similar as the author would have his readers believe. The ethics of religion speaks of ways of behaving that are required regardless of the demands of the confronting situation. But psychological science, especially the socially oriented type, must deal with the appropriateness of the specific behavior to the demands of the moment—it must be field-oriented. The confusion and distortion in this realm are amply demonstrated in the final section. The author summarizes common abuses of child rearing by pairing such harmfuls as overprotection versus underprotection, training too early versus training too late, too high standards versus inadequate standards, etc. Each of these suggests the relativity of parental behavior to the readiness or requirements of the child. But several pages later he speaks of the golden mean of balance as a secure guide. The golden mean of protection may be appropriate for the average child, but it is by no means pertinent to the exceptional child, who may need much more or much less help. It must firmly be objected that the author equates piety with scientific knowledge.

Third, the author fails to recognize the internal contradiction of his plea that man's salvation rests upon a concerted attack upon the level of mental health of the parents and children today. Once more the author's religious zeal springs forth. The point is much debated in the social sciences today, and no real conclusion has been reached, but the paradox must still be noted: If people, especially parents, were prepared psychologically to receive and act upon advice and education relative to the handling of their children, they would also be well enough along the way to controlling their own hostilities and the problem would not exist. This is the bitter truth that World War I thrust upon the optimists who trusted to education for the end of all wars. Education is fine for those who wish it, but the people who need it most are also least capable of using it. As in the psychotherapeutic situation, in which the more neurotic the patient the more difficult it is to conduct the therapy, so too in society as a whole; the most hostile men are least receptive to suggestions for democratic cooperation. The goal we will all admit is human happiness; the means to this goal, however, must be more clearly understood if psychiatry wishes to contribute its total resources to the general welfare. The author has failed to do this, for he has not reckoned with the well-known resistance, which is as much found outside the analytic office as inside it.

Psychiatry's contribution to society will not be the one the author implicitly proposes, that psychiatry should lead the attack on the world's problems. Rather, if it learns more modesty, psychiatry can cooperate with other social forces by helping us all to distinguish between true solutions and solutions that arise primarily from personal distortions. By prescribing emotional maturity as a goal independently of the general strivings in our culture, the author inhibits such cooperation.

The Legacy of Sigmund Freud. By Jacob A. Arlow, M.D. Price, $2.00. Pp. 96. International Universities Press, Inc., 227 W. 13th St., New York 11, 1956.

When a famous man dies, it seems to be common practice for a number of authors to rush to press with critical evaluations of the contributions of the man and his imprint on culture, society, science, history, and life. Now, one hundred years after the birth of Freud, and a very short seventeen years after his death, Arlow has written a small book about Freud that assiduously and with skill avoids the usual pitfall, namely, a complete evaluation at a time when it is impossible to make one because an insufficient period has elapsed to let his work settle into its proper niche in the panorama of history.

An outgrowth of the work of the Freud Centenary Committee of the American Psychoanalytic Association, Arlow's monograph attempts to show us some measure of the genius of Freud, and to demonstrate some of the rich legacy he has left us, in the form of his discoveries, knowledge, and thinking. By selecting representative samplings of Freud's work, by organizing them according to various interests and fields (such as biology, neurology, dreams, therapy, religion, mythology, aesthetics, anthropology, and sociology), and by presenting a number of ideas as they developed chronologically in Freud's work and mind, Arlow has given us a simple and understandable appreciation of Freud, his efforts, the scope and breadth of his interests and areas of contribution, and the development of his thought. He has given us, in fact, a brief biography of Freud's thinking.

Addressed to the general public, it is perhaps by virtue of its brevity too sketchy to be totally understood and appreciated, but it certainly will titillate the appetite of most to pursue the subject. As a book for those in any part of the field of mental health, this capsule of Freudian thought will be stimulating, create a heightened perspective, and increase our understanding of otherwise complex material. The putting of many early—and now abandoned—ideas into an historical perspective serves to clarify areas often seemingly contradictory.

Written with great lucidity, and attractively published, it is a pleasure to read and to own. In his preface, Arlow hopes "that, from these pages, there will emerge an appreciation of the richness of Freud's genius, the development of his thought, and the manifold implications of his thought to the science of psychoanalysis of which he was the founder and the principal developer." In this he had succeeded well.

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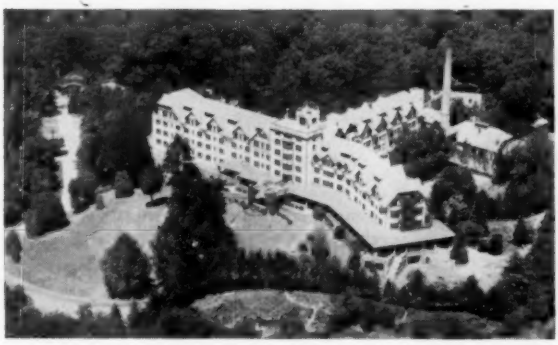

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1. Hoffman, J.L.: in Chlorpromazine and Mental Health, Philadelphia, Lea & Febiger, 1955.

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